

# ORGANIC SYNTHESSES

AN ANNUAL PUBLICATION OF SATISFACTORY  
METHODS FOR THE PREPARATION  
OF ORGANIC CHEMICALS

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## ORGANIC SYNTHESSES

*An Annual Publication of Satisfactory  
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Organic Chemicals*

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## PREFACE TO VOLUME XIV

The index of the present volume includes those of Volumes X, XI, XII, and XIII but not those of earlier volumes; and in the text, citations are made only to Org. Syn. **10**, **11**, **12**, and **13** and to Coll. Vol. **1**.

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BY

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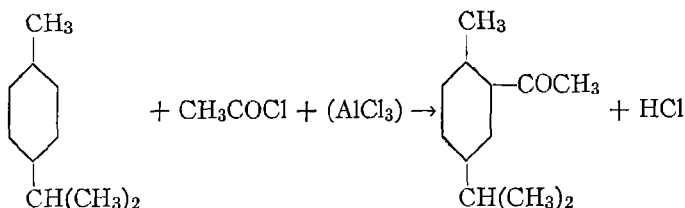
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# ORGANIC SYNTHESSES

## I

### ACETO-*p*-CYMENE

(2-Methyl-5-*iso*-propylacetophenone)



Submitted by CHARLES F. H. ALLEN.

Checked by REYNOLD C. FUSON and CHARLES F. WOODWARD.

#### 1. Procedure

A 1-l. three-necked flask is fitted with a dropping funnel, a stirrer, a thermometer for reading low temperatures (Note 1), and a condenser, to the upper end of which is attached a tube for disposing of the hydrogen chloride evolved (Note 2). A mixture of 200 cc. of carbon disulfide and 180 g. (1.35 moles) of anhydrous aluminum chloride is placed in the flask which is then immersed in an ice-salt freezing mixture and stirred very vigorously until the temperature of the mixture is  $-5^{\circ}$  or below. A mixture of 175 g. (205 cc., 1.3 moles) of *p*-cymene and 110 g. (100 cc., 1.4 moles) of acetyl chloride is added from the dropping funnel at such a rate that the temperature never rises above  $5^{\circ}$ . The time required for the addition is about three and one-third hours (Note 3). The mixture is allowed to stand overnight and is then poured upon 1 kg. of cracked

ice to which 200 cc. of concentrated hydrochloric acid has been added. The mixture is extracted with three 700-cc. portions of ether; the ether solution is dried over anhydrous calcium chloride and distilled at ordinary pressure from a Claisen flask provided with an indented column, until the temperature reaches 190°. The material that remains in the flask is fractionally

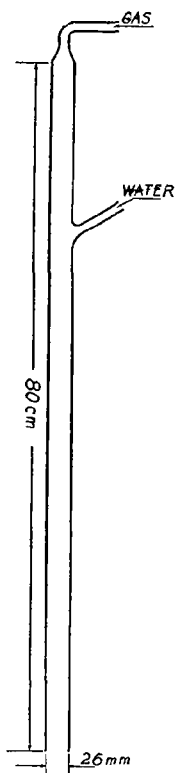


FIG. 1.

distilled twice under diminished pressure. The principal fraction is aceto-*p*-cymene, a pale yellow oil boiling at 124–125°/12 mm. (155–157°/30 mm.). It weighs 115–125 g. (50–55 per cent of the theoretical amount) (Note 4). About 50 g. of cymene is recovered (Note 5), and there is a small amount (10–12 g.) of residual oil left in the flask (Note 6).

## 2. Notes

1. Since it is impossible to read that part of the thermometer scale which extends into the reaction flask, a thermometer should be used which when in position has the zero point above the stopper of the flask. A thermometer reading from –50° to +50° is recommended.

2. A gas trap of the type shown in Fig. 1 is suitable for this purpose.

3. After about two-thirds of the mixture has been added the rate of addition may be increased somewhat. The time required for the addition depends on the efficiency of the cooling and stirring; the latter must be vigorous. With one-half of these amounts in a 500-cc. flask, the time required is only about one and

one-third hours since under these conditions it is easier to control the temperature.

4. From the first fractionation a fraction boiling over a 20° range is taken as crude ketone; e.g., at 28–30 mm. the fraction is taken which boils at 145–165°. Much trouble is

caused by the tendency of the ketone to become superheated.

5. Acetyl chloride gives a better yield and less high-boiling residue than does acetic anhydride.

6. This procedure has also been used successfully in the acetylation of cumene and *tert.*-butylbenzene. At the low temperatures employed there is very little decomposition, as is shown by the small amount of high-boiling residue.

### 3. Methods of Preparation

Aceto-*p*-cymene can be prepared by the action of acetyl chloride on *p*-cymene in the presence of anhydrous aluminum chloride<sup>1</sup> or ferric chloride.<sup>2</sup>

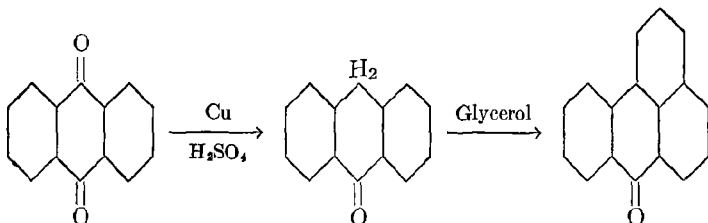
<sup>1</sup> Lacourt, Bull. soc. chim. Belg. **38**, 17 (1929); Claus, Ber. **19**, 232 (1886); Klages and Lickroth, *ibid.* **32**, 1563 (1899); Verley, Bull. soc. chim. [3] **17**, 910 (1897).

<sup>2</sup> Meissel, Ber. **32**, 2421 (1899).



## II

### BENZANTHRONE



Submitted by L. C. MACLEOD and C. F. H. ALLEN.

Checked by L. F. FIESER and MAX TISHLER.

#### 1. Procedure

In a 2-l. three-necked flask fitted with a mechanical stirrer and thermometer, 72 g. (0.35 mole) of anthraquinone is dissolved in 1060 cc. of concentrated sulfuric acid by stirring at room temperature, and 42 cc. of water is then added to the red solution (Note 1). The flask is immersed up to the neck in an oil bath, and 48 g. (0.76 mole) of precipitated copper (Note 2) is added over a period of one and one-half hours, keeping the reaction mixture at a temperature of 38–42°, if necessary by external heating, until all of the copper has dissolved, which requires about three hours (Note 3).

A mixture of 96 g. (1.04 moles) of glycerol (Note 4) and 96 cc. of water is slowly introduced in the course of thirty minutes and the temperature is allowed to rise to 85–90°. The mixture is carefully heated to 120° during one and one-half hours, in such a way that the temperature rises uniformly at a rate of 1° every three minutes (Note 5). A temperature of 118–120° is maintained for an additional three-hour period, and the mixture cooled to 70–80° and carefully poured with stirring into 4 l. of boiling water (Note 6). Spattering is avoided by pouring the acid

mixture down the walls of the beaker while stirring. The suspension is boiled for a few minutes and preferably allowed to stand for several hours before being filtered.

The dark green benzanthrone is filtered on a large Büchner funnel, washed well with water, and boiled for thirty to forty minutes with 1.2 l. of 1 per cent sodium hydroxide solution. The product is filtered, washed free of the dark-colored liquor, and dried at 120°; weight, 67-71 g.; benzanthrone content, about 87 per cent. The crude material is boiled with 500 cc. of tetrachloroethane (technical), in which all but about 8 g. of a black char easily dissolves. The solution is boiled under reflux for fifteen minutes with 25 g. of a decolorizing carbon, and then filtered while hot through a Büchner funnel directly into a 2-l. round-bottomed, long-necked flask, washing the residue with hot tetrachloroethane (100-150 cc.) until the filtrate is colorless. After adding 400-500 cc. of hot water, the solvent is removed by steam distillation, a process which requires but little time. The benzanthrone left as a residue is filtered and dried at 120°. The yield of yellow solid, which melts at 168-170° and is pure enough for many purposes, is 56-60 g. (70-75 per cent of the theoretical amount).

In order to secure a pure product the above material is dissolved in 175 cc. of tetrachloroethane by boiling and the solution is boiled under reflux for fifteen minutes with 12 g. of decolorizing carbon, and then filtered by suction into an Erlenmeyer flask, washing the charcoal with about 50 cc. of hot solvent. The filtrate is kept hot, treated with 750 cc. of boiling alcohol, and set aside to crystallize. The benzanthrone separates as pure yellow needles melting at 170-171°; yield, 48-52 g. (60-65 per cent of the theoretical amount) (Note 7).

## 2. Notes

1. The solution of the anthraquinone is slower if the water is added at the outset.

2. The precipitated copper is prepared as on page 67, using twice the quantities given.

3. The mixture becomes yellow-brown in color and some anthranol separates, but any unreacted copper can be seen on the bottom of the flask if the stirring is stopped for a few minutes.

4. The glycerol is a commercial, anhydrous product.

5. The heating must be done very carefully and the temperature must never be allowed to rise above 120°. At higher temperatures much material is lost by charring.

6. A more granular and easily filterable product is obtained than when cold water is used.

7. On recovery of the tetrachloroethane by steam distillation of the mother liquor, there is obtained a small additional quantity of material (5 g.), but it is quite dark and of poor quality.

### 3. Methods of Preparation

Benzanthrone has been prepared by three general methods, the first of which is generally regarded as the best: (1) by heating a reduction product of anthraquinone with sulfuric acid and glycerol,<sup>1</sup> or with a derivative of glycerol,<sup>2</sup> or with acrolein.<sup>3</sup> The anthraquinone is usually reduced in sulfuric acid solution, just prior to the reaction, by means of aniline sulfate,<sup>1b</sup> iron,<sup>1c</sup> or copper.<sup>1d</sup> It has also been prepared (2) by the action of aluminum or ferric chloride on phenyl- $\alpha$ -naphthyl ketone,<sup>4</sup> and (3) from 1-phenylnaphthalene-2-carboxylic acid.<sup>5</sup>

The above procedure, except for the method of purification, is based upon a recent patent.<sup>1d</sup>

<sup>1</sup> (a) Bally, Ber. **38**, 194 (1905), Ger. pat. 176,018; (b) Bally and Scholl, Ber. **44**, 1665 (1911); (c) Russ. pat. 18,741 (1931) [Chem. Zentr. **102**, II, 1759 (1931)]; (d) U. S. pat. 1,626,392 (1927); (e) Bacharach and Cauliff, U. S. pat. 1,893,575 (1933).

<sup>2</sup> Ger. pat. 204,354 [Frdl. **9**, 818 (1908-9)].

<sup>3</sup> Cross and Perkin, J. Chem. Soc. **1927**, 1297.

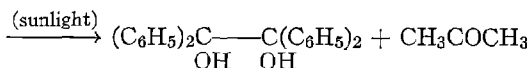
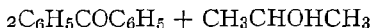
<sup>4</sup> Scholl and Seer, Ann. **394**, 116 (1912); Monatsh. **33**, 1 (1912); Ger. pat. 239,761.

<sup>5</sup> Schaarschmidt, Ber. **50**, 295 (1917).



### III

#### BENZOPINACOL



Submitted by W. E. BACHMANN.

Checked by JOHN R. JOHNSON and H. R. SNYDER.

#### 1. Procedure

A mixture of 150 g. (0.824 mole) of benzophenone (Org. Syn. Coll. Vol. **1**, 89) (Note 1), one drop of glacial acetic acid (Note 2), and 665 g. (850 cc., 11 moles) of *iso*-propyl alcohol (Note 3) in a 1-l. round-bottomed flask is warmed to 45°. The flask is closed with a tight cork firmly wired or tied in place, and is supported in an inverted position in a tripod and exposed to direct sunlight. After three to five hours of bright sunshine crystals of benzopinacol begin to appear; after eight or ten days of exposure, depending upon the intensity of the light (Note 4), the flask is filled with crystals of benzopinacol. The solution is chilled in ice and the crystalline product is filtered with suction, washed with a small quantity of *iso*-propyl alcohol, and allowed to dry in the air. The filtrate is reserved for subsequent reductions (see below). The yield of practically pure benzopinacol, m.p. 188–190° (Note 5), is 141–142 g. (93.5–94 per cent of the theoretical amount). The product is sufficiently pure for most purposes. It may be crystallized by dissolving it in 1000 cc. of hot benzene, filtering, and adding 400 cc. of hot ligroin (b.p. 90–100°) to the hot filtrate. After cooling in ice and filtering there is obtained 129–130 g. of purified product. The melting point is not changed by this purification.

To the *iso*-propyl alcohol filtrate is added another 150-g. portion of benzophenone and the solution is exposed to sunlight as in the first reduction. The benzopinacol which separates is filtered and dried. The yield in the second and subsequent runs is 142-143 g. (94-95 per cent of the calculated amount). This procedure can be repeated with the same filtrate until six or seven portions (900-1050 g.) of benzophenone have been reduced.

## 2. Notes

1. Although a practical grade of benzophenone can be used in this preparation, it is better to use material that has been recrystallized from alcohol.

2. No more than one drop of acetic acid should be used. The acid is added to insure the removal of traces of alkali, which cause decomposition of the pinacol into benzophenone and benzohydrol.

3. If *iso*-propyl alcohol is not available, absolute ethyl alcohol can be used. With ethyl alcohol the reaction is slower and a yellow solution is obtained; nevertheless, the crystals of benzopinacol are colorless.

4. About five clear bright days are required to complete the reduction. The reaction can be interrupted at any time, the crystals filtered off, and the filtrate then exposed further.

5. Since the pinacol decomposes near its melting point the latter will vary with the rate of heating. The temperatures reported here were obtained by slow heating; if the tube is placed in a bath at 150° and heated rapidly, the observed melting or decomposition point is 193-195°.

## 3. Methods of Preparation

Benzopinacol has been prepared by the action of phenylmagnesium bromide on benzil<sup>1</sup> or methyl benzilate.<sup>1</sup> Usually it has been obtained by reduction of benzophenone, the reducing agents being zinc and sulfuric acid<sup>2</sup> or acetic acid,<sup>3</sup> aluminum amalgam,<sup>4</sup> and magnesium and magnesium iodide.<sup>5</sup> The present

method is based on a study by Cohen <sup>6</sup> of the photochemical reaction discovered by Ciamician and Silber.<sup>7</sup>

<sup>1</sup> Acrec, Ber. **37**, 2761 (1904).

<sup>2</sup> Linnemann, Ann. **133**, 26 (1865).

<sup>3</sup> Zagumenny, Ber. **14**, 1402 (1881).

<sup>4</sup> Cohen, Rec. trav. chim. **38**, 75 (1919).

<sup>5</sup> Gomberg and Bachmann, J. Am. Chem. Soc. **49**, 241 (1927).

<sup>6</sup> Cohen, Rec. trav. chim. **39**, 243 (1920).

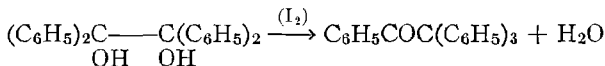
<sup>7</sup> Ciamician and Silber, Ber. **33**, 2911 (1900).





## IV

### β-BENZOPINACOLONE



Submitted by W. E. BACHMANN.

Checked by JOHN R. JOHNSON and H. R. SNYDER.

#### 1. Procedure

In a 1-l. round-bottomed flask provided with a reflux condenser is placed a solution of 1 g. of iodine in 500 cc. of glacial acetic acid. One hundred grams (0.273 mole) of benzopinacol (Note 1) is added, and the flask is heated over a wire gauze, with shaking, until the solution boils gently. It is then refluxed for five minutes during which the solid benzopinacol disappears completely and a clear red solution is obtained (Note 2). The solution is transferred at once to a 1-l. beaker and upon cooling the benzopinacolone separates in fine threads. The product is filtered with suction, washed with two or three 60-cc. portions of cold glacial acetic acid until colorless, and dried. The filtrate is reserved for subsequent preparations. The yield of practically pure benzopinacolone melting at 178–179° is 90–91 g. (95–96 per cent of the theoretical amount). If a purer product is desired the material may be dissolved in 450 cc. of hot benzene, filtered, and treated with 250 cc. of hot ligroin (b.p. 90–100°). After cooling in ice the benzopinacolone is filtered and dried. The purified product weighs 82–83 g. and melts at 179–180°.

To the acetic acid filtrate is added another 100-g. portion of benzopinacol and the reaction is carried out in the same way. The yield of benzopinacolone in the second and subsequent runs is 94–94.5 g. (98–99 per cent of the theoretical amount).

This procedure can be repeated in the same filtrate until 500 g. of the pinacol has been rearranged.

## 2. Notes

1. The benzopinacol obtained by photochemical reduction of benzophenone (p. 8) may be used directly without purification.

2. Frequently the benzopinacolone begins to crystallize in the boiling solution during the last minute of heating.

## 3. Methods of Preparation

$\beta$ -Benzopinacolone has been prepared by rearrangement of benzopinacol. The rearrangement has been carried out by heating benzopinacol with benzoyl chloride,<sup>1</sup> with acetyl chloride,<sup>2</sup> with acetic acid at 180–200°,<sup>2</sup> with dilute sulfuric acid at 180–200°,<sup>2</sup> and with concentrated hydrochloric acid at 200°. The present procedure is based on the method described by Gomberg and Bachmann.<sup>3</sup>

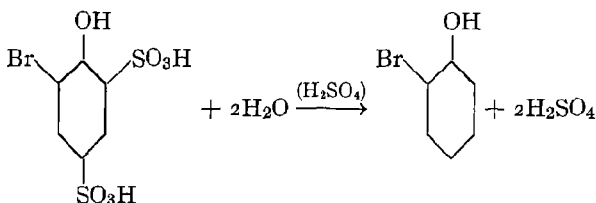
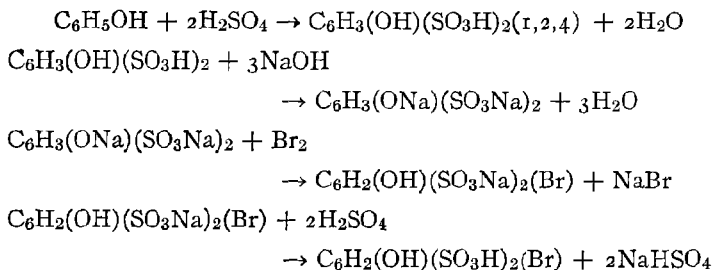
<sup>1</sup> Linnemann, Ann. **133**, 28 (1865).

<sup>2</sup> Thörner and Zincke, Ber. **10**, 1475 (1877).

<sup>3</sup> Gomberg and Bachmann, J. Am. Chem. Soc. **49**, 246 (1927).

## V

### o-BROMOPHENOL



Submitted by RALPH C. HUSTON and MUREL M. BALLARD.

Checked by LOUIS F. FIESER and MAX TISHLER.

### 1. Procedure

IN a 3-l. three-necked flask is placed a mixture of 94 g. (1 mole) of phenol and 350 g. (190 cc., 3.4 moles) of concentrated sulfuric acid, and the mixture is heated on a boiling water bath for three hours with constant mechanical stirring. At the end of this time the reaction mixture is cooled by replacing the boiling water bath by an ice bath. When it has been cooled to room temperature, the solution is made alkaline by the careful addition of a solution of 280 g. (7 moles) of sodium hydroxide in 700 cc. of water (Note 1). This must be done slowly and with good cooling to prevent boiling. A solid salt, which at first separates, largely dissolves at a later stage.

The alkaline solution is cooled to room temperature and, with the stirrer still in constant operation, and after inserting a thermometer, 160 g. (1 mole) of bromine is added from a dropping funnel in the course of twenty to thirty minutes. During this operation the temperature is allowed to rise to 40-50°. Stirring is continued for one-half hour after all of the bromine has been added. The solution should still be alkaline and should contain only a small amount of suspended material.

In order to evaporate the solution, the flask is then placed in an oil bath, which is brought to a temperature of 150-155°. As soon as solid material begins to separate, the mixture will bump badly unless a rather rapid current of air is passed through the reaction mixture. This has the further advantage of hastening the evaporation (Note 2). The heating is continued until a thick, pasty, gray mass is left as a residue, the process requiring thirty to forty minutes. The mixture is allowed to cool and then made strongly acid by the addition of 800 cc. of concentrated sulfuric acid. This must be done slowly and under a hood on account of the rapid evolution of hydrogen bromide.

The flask is then heated in an oil bath maintained at a temperature of 190-210° and the mixture subjected to steam distillation. The sulfonate groups are hydrolyzed in this process and the bromophenol passes over as a heavy, colorless or pale yellow oil. In about one hour the distillate is clear. The product is extracted with ether, the ether is removed by distillation from the steam bath, and the residue is distilled at atmospheric pressure (Note 3). The fraction boiling at 194-200° represents practically pure o-bromophenol. The yield is 70-75 g. (40-44 per cent of the theoretical amount) (Note 4). o-Bromophenol is a colorless liquid with a very characteristic odor. It is rather unstable and decomposes on standing, becoming brown or red in color.

## 2. Notes

1. Too great an excess of water in the reaction mixture appears to result in the formation of higher bromination products.

Insufficient water causes the reaction mixture to solidify during bromination, preventing efficient agitation.

2. A small amount of tribromophenol is eliminated in the evaporation, the substance being volatile with steam.

3. Distillation should be as rapid as possible, as the *o*-bromophenol is somewhat unstable and decomposes rapidly at the high temperature. Distillation at reduced pressure has not been found to offer much improvement.

4. The rather large residue of higher-boiling material probably contains higher bromination products of phenol.

### 3. Methods of Preparation

*o*-Bromophenol has been prepared by the direct bromination of phenol in various solvents and with various brominating agents.<sup>1</sup> It has been obtained by the decarboxylation of 2-bromo-3-hydroxybenzoic acid,<sup>2</sup> by the diazotization of *o*-bromoaniline,<sup>3</sup> and from *o*-aminophenol by the Sandmeyer reaction.<sup>4</sup> The method given here is an adaptation of that of Takagi and Kutani.<sup>5</sup>

<sup>1</sup> Hubner and Brenken, Ber. **6**, 171 (1873); Ger. pat. 76,597 [Frdl. **3**, 845 (1890)]; Dinwiddie and Kastle, Am. Chem. J. **46**, 502 (1911); Skraup and Beifuss, Ber. **60**, 1077 (1927); Likhoshersov, J. Russ. Phys. Chem. Soc. **61**, 1019 (1925).

<sup>2</sup> Lellmann and Grothmann, Ber. **17**, 2726 (1884).

<sup>3</sup> Fittig and Mayer, *ibid.* **8**, 362 (1875).

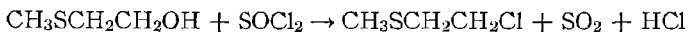
<sup>4</sup> Mendola and Streatfield, J. Chem. Soc. **73**, 685 (1898).

<sup>5</sup> Takagi and Kutani, J. Pharm. Soc. Japan, No. 517, 260 (1925).



## VI

### $\beta$ -CHLOROETHYL METHYL SULFIDE



Submitted by W. R. KIRNER and WALLACE WINDUS.

Checked by H. T. CLARKE and S. GURIN.

#### 1. Procedure

IN a 1-l. three-necked flask are mixed 150 g. (1.63 moles) of  $\beta$ -hydroxyethyl methyl sulfide (p. 54) (Note 1) and 200 g. of dry chloroform (Note 2). The flask is placed on a steam bath and is fitted with a dropping funnel, a mechanical stirrer, and a condenser. The condenser is fitted with a trap to remove the vapors of hydrogen chloride and sulfur dioxide (page 2). A solution of 204 g. (1.7 moles) (Note 3) of thionyl chloride in 200 g. (135 cc.) of dry chloroform is added dropwise to the  $\beta$ -hydroxyethyl methyl sulfide over a period of about two hours (Note 4). The reaction mixture is stirred vigorously during this addition and for about four hours after the addition is complete. The chloroform is distilled on the steam bath and the residue is distilled under reduced pressure. The yield is 135-153 g. (75-85 per cent of the theoretical amount) of a product boiling at 55-56°/30 mm. (Note 5).

#### 2. Notes

1. Quantities of material seven times as large as the above may be used without decreasing the yield of the product.

2. The chloroform is dried by distillation, and the fraction boiling at 60-61° is used.

3. The thionyl chloride is redistilled, and the fraction boiling at 76-78° is employed.

4. The reaction mixture is heated once when about half the thionyl chloride has been added in order to keep the chloroform refluxing gently. Heating after the complete addition of the thionyl chloride is undesirable.

5.  $\beta$ -Chloroethyl methyl sulfide is a vesicant and must be handled with care. It boils at  $140^{\circ}$  under atmospheric pressure.

### 3. Methods of Preparation

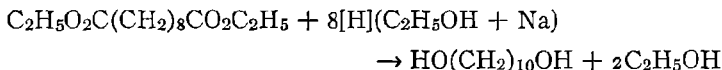
The above method is essentially that recently described in the literature.<sup>1</sup>

<sup>1</sup> Kirner, J. Am. Chem. Soc. **50**, 2452 (1928).



## VII

### DECAMETHYLENE GLYCOL



Submitted by R. H. MANSKE.

Checked by W. H. CAROTHERS and W. L. McEWEN.

#### 1. Procedure

To a solution of 65 g. (0.25 mole) of ethyl sebacate in 800 cc. of absolute ethyl alcohol (Note 1) contained in a 3-l. round-bottomed flask, to which is attached a 60-cm. bulbed reflux condenser protected by a calcium chloride drying tube, is added 70 g. (3 gram atoms) of sodium in large pieces in one lot. The somewhat vigorous reaction is easily kept under control by immersing the entire flask in a mixture of crushed ice and water. In a short time the reaction has subsided somewhat; the flask is then removed from the cooling mixture, and the reaction is allowed to proceed without external cooling. Reduction is completed by heating the mixture on a steam bath until all the sodium has dissolved. The partly cooled mixture is diluted with 300 cc. of water and the alcohol distilled off until no further distillate is obtained at steam-bath temperatures. The remaining small amount of alcohol is removed by gently applying a suction from a water pump. The residue is diluted with about 600 cc. of hot water, and the mixture is allowed to cool without being disturbed. The separated oil solidifies to a solid cake from which the lower aqueous layer is easily decanted. The solid is washed once with a little cold water, drained as completely as possible, and dried by heating in the flask on a steam bath under reduced pressure. The residue is extracted with four successive portions of hot benzene, each of 250 cc. The united extract is clarified with a little charcoal, filtered, and most of the benzene distilled. The residue (about 60 cc.) is taken up in alcohol (about 200 cc.), filtered again, evapor-

ated to a small volume (about 60 cc.) and treated with an equal volume of hot benzene. On slow cooling the mixture sets to a solid mass of large crystals, which are filtered and washed with ether. The yield of this product which melts at  $72-74^{\circ}$  corr. is 32-33 g. (73-76 per cent of the theoretical amount). When making several runs or a larger single run, the combined mother liquors may be evaporated free of solvent and the residue distilled under reduced pressure. The distillate on recrystallization from alcohol-benzene yields, however, only 5 to 7 grams of pure glycol per mole of sebacic ester (Notes 2 and 3).

## 2. Notes

1. The alcohol must be perfectly dry. Any water present causes immediate saponification of the ester with a consequent loss of yield. An excellent method for preparing really anhydrous alcohol is that of Smith (J. Chem. Soc. 1927, 1288), or the modification proposed by Manske (J. Am. Chem. Soc. 53, 1106 (1931)).

2. The general method of Bouveault and Blanc has been used extensively for the preparation of glycols. Various modifications of detail have been suggested. Most of them are probably trivial or immaterial. In the experience of the checkers the rapid addition of the alcohol-ester mixture to the sodium gives results approximately equal to those described above (see J. Am. Chem. Soc. 52, 5287 (1931)), but mechanical stirring of the reaction mixture seriously reduces the yield. The method used for isolating the glycol must be adapted to the properties of the glycol. At least for small runs the method of crystallization described here is the most suitable for decamethylene glycol. Lower members of the series are less readily crystallized. C. S. Marvel in a private communication has pointed out that for these glycols continuous ether extraction is the best method, and this has been used for hexamethylene glycol with success by the checkers.

3. Using this procedure the checkers have prepared the following glycols.

	Yield, Per cent
Heptamethylene glycol..... b.p. 143-146°/8 mm....	88
Nonamethylene glycol..... b.p. 147-150°/2 mm....	71
Undecamethylene glycol..... m.p. 48-50°.....	57
Tridecamethylene glycol..... m.p. 75-77°.....	88
Tetradecamethylene glycol..... m.p. 83-85°.....	61
Octadecamethylene glycol..... m.p. 96-98°.....	54

The heptamethylene glycol was separated by continuous ether extraction from the alkaline reduction solution after the latter had been diluted and distilled to remove the alcohol. The nonamethylene glycol was separated from the alkaline liquor by decantation (as above) and distilled. All the others were crystallized from benzene (without alcohol). Equally successful results have also been obtained with larger runs (e.g., 0.5 mole of ester).

### 3. Methods of Preparation

Decamethylene glycol has been prepared by the reduction of dimethyl sebacate<sup>1</sup> and diethyl sebacate<sup>2</sup> with sodium and ethyl alcohol; by the reduction of sebacamide with sodium and amyl alcohol;<sup>3</sup> and by the reduction of dimethyl sebacate with sodium and liquid ammonia in absolute alcohol.<sup>4</sup> The reduction of esters with sodium and alcohol has also been applied to the preparation of many other glycols.<sup>5</sup>

More recently methods have been developed for the catalytic hydrogenation of sebacic esters to decamethylene glycol.<sup>6</sup>

<sup>1</sup> Bouveault and Blanc, *Compt. rend.* **137**, 329 (1903); *Bull. soc. chim.* [3] **31**, 1205 (1904); *Ger. pat.* 164,294 [*Frdl.* 8, 1260 (1905)]; Chuit, *Helv. Chim. Acta* **9**, 264 (1926).

<sup>2</sup> Franke and Kienberger, *Monatsh.* **33**, 1191 (1912); Carothers, Hill, Kirby and Jacobson, *J. Am. Chem. Soc.* **52**, 5287 (1931).

<sup>3</sup> Scheuble, *Monatsh.* **24**, 623 (1903); Scheuble and Loeb, *ibid.* **25**, 344 (1904); Alberti and Smieciuszewski, *ibid.* **27**, 411 (1906).

<sup>4</sup> Chablay, *Compt. rend.* **156**, 1021 (1913); *Ann. chim.* [9] **8**, 216 (1917).

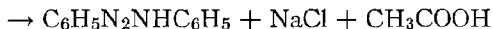
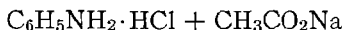
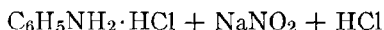
<sup>5</sup> Böeseken, *Rec. trav. chim.* **34**, 100 (1915); Müller, *Monatsh.* **49**, 27 (1928); Bouveault and Blanc, *Compt. rend.* **137**, 329 (1903); *Bull. soc. chim.* [3] **31**, 1204 (1904); *Ger. pat.* 164,294 [*Frdl.* 8, 1260 (1905)]; Franke and Lieben, *Monatsh.* **35**, 1433 (1914); Müller and Sauerwald, *ibid.* **48**, 523 (1927); Chuit, *Helv. Chim. Acta* **9**, 264 (1926); Chuit, Boelsing, Hausser and Malet, *ibid.* **10**, 167 (1927); Chuit and Hausser, *ibid.* **12**, 850 (1929).

<sup>6</sup> Folkers and Adkins, *J. Am. Chem. Soc.* **54**, 1146 (1932).



## VIII

### DIAZOAMINO BENZENE



Submitted by W. W. HARTMAN and J. B. DICKEY.

Checked by C. R. NOLLER and C. R. KEMP.

#### 1. Procedure

IN a 5-l. flask fitted with a mechanical stirrer and a dropping funnel are placed 1 kg. of cracked ice, 1500 cc. of water, 279 g. (3 moles) of a technical grade of aniline, and 458 g. (387 cc., 4.5 moles) of concentrated hydrochloric acid (sp. gr. 1.18). The stirrer is started, and a solution of 109 g. (1.5 moles) of 95 per cent sodium nitrite in 250 cc. of water is added over a period of fifteen minutes. The reaction mixture is then stirred for fifteen minutes, and a solution of 422 g. (3.1 moles) of crystalline sodium acetate dissolved in 800 cc. of water is added over a period of five minutes. A yellow precipitate of diazoaminobenzene begins to form at once. Stirring is continued for forty-five minutes, keeping the temperature below 20° (Note 1). The yellow diazoaminobenzene is filtered on a 19-cm. Büchner funnel (Note 2), washed with 5 l. of cold water, and then sucked as dry as possible and spread out on a sheet of paper to dry (Note 3). The product thus obtained is dissolved in 4 l. of boiling ligroin (b.p. 60–90°) (Note 4), filtered, and allowed to cool to room temperature and stand overnight. When crystallization is com-

plete, the yellow crystals are filtered on a 19-cm. Büchner funnel, washed with 500 cc. of cold ligroin (b.p. 60–90°), and dried at room temperature. The yield of yellow crystals melting at 92–94° is 242–251 g. (82–85 per cent of the theoretical amount) (Note 5). If a product of greater purity is desired, the diazoaminobenzene is dissolved in 4 l. of boiling ligroin (b.p. 60–90°) and crystallized as before. The yield of recrystallized diazoaminobenzene melting at 94–96° is 204–218 g. (69–73 per cent of the theoretical).

## 2. Notes

1. The temperature noted is not known to be the maximum temperature at which the reaction may be run.

2. A centrifuge of suitable size is preferable if available.

3. A rubber dam is fitted over the top of the Büchner funnel and held in place by rubber bands in order to remove as much of the water as possible.

4. Prolonged heating of the diazoaminobenzene with ligroin causes decomposition. For this reason it is well to heat the ligroin to boiling before it is added to the product to be crystallized. Solution is effected as rapidly as possible. In the event that the crude diazoaminobenzene is not dry, a layer of water will separate at the bottom of the flask. This should be removed as completely as possible before filtering the hot ligroin solution.

5. An additional crop of crystals weighing 20–25 g. and melting at 79–83° can be obtained by evaporating the mother liquors to 1 l. and chilling in an ice bath.

6. The size of the run may be halved; an actual run with half quantities gave 125 g.

## 3. Methods of Preparation

Diazoaminobenzene has been prepared by the action of sodium nitrite on aniline sulfate;<sup>1</sup> by the action of sodium nitrite on aniline hydrochloride;<sup>2</sup> by the action of sodium nitrite and sodium acetate on aniline hydrochloride;<sup>3</sup> by the action of ammonium nitrate and hydrogen sulfide on aniline hydrochloride in the presence of iron;<sup>4</sup> and by the action of amyl nitrite on aniline.<sup>5</sup>

Diazoaminobenzene has also been prepared by the action of nitrous acid gas on aniline in alcohol;<sup>6</sup> by the action of silver nitrite on aniline hydrochloride;<sup>7</sup> and together with phenylurea by the action of nitrosophenylurea on aniline in methyl alcohol.<sup>8</sup> Niementowski and Roszkowski<sup>9</sup> have reported studies on the diazotization of aniline, aniline hydrochloride, and aniline sulfate with sodium nitrite and silver nitrite. The procedure described is adapted from that of Fischer.<sup>3</sup>

<sup>1</sup> Stadel and Bauer, Ber. 19, 1952 (1886).

<sup>2</sup> Martius, Z. Chem. 1886, 381; Curtius, Ber. 23, 3033 (1890); Vaubel, Chem. Ztg. 35, 1238 (1911).

<sup>3</sup> Fischer, Ber. 17, 641 (1884).

<sup>4</sup> Vaubel, Chem. Ztg. 37, 637 (1913).

<sup>5</sup> Meyer and Ambuhl, Ber. 8, 1073 (1875).

<sup>6</sup> Griess, Ann. 121, 257 (1862).

<sup>7</sup> Niementowski and Roszkowski, Z. physik. Chem. 22, 158 (1897).

<sup>8</sup> Haager, Monatsh. 32, 1089 (1911).

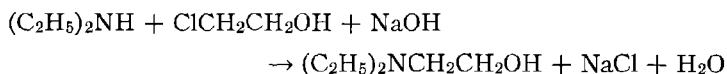
<sup>9</sup> Niementowski and Roszkowski, Z. physik. Chem. 22, 145 (1897).





## IX

### $\beta$ -DIETHYLAMINOETHYL ALCOHOL



Submitted by W. W. HARTMAN.

Checked by W. H. CAROTHERS and W. L. McEWEN.

#### 1. Procedure

IN a 2-l. flask provided with a reflux condenser and a dropping funnel is placed 380 g. (5.2 moles) of diethylamine (b.p. 52–60°). The diethylamine is heated to boiling over a steam bath, and 320 g. (4 moles) of ethylene chlorohydrin is added from the dropping funnel during the course of about one hour. Heating is then continued for eight hours more. The reaction mixture is allowed to cool, and a solution of 230 g. of sodium hydroxide in 350 cc. of water is added fairly rapidly with constant shaking. Two layers form immediately, and sodium chloride is precipitated. The latter is dissolved by the addition of 400 cc. of water, and then 500 cc. of benzene is added and the mixture is stirred mechanically for five minutes. The benzene layer is separated and the aqueous layer is extracted three times more, using 500 cc. of benzene for each extraction. The combined benzene extracts are dried over solid potassium carbonate (about 100 g.) with mechanical stirring until the turbidity of the solution has disappeared. The solution is distilled from a 3-l. flask provided with a 50-cm. column (packed with glass or carborundum) and a thermometer dipping in the liquid. Distillation is continued until the temperature of the liquid reaches 100° and that at the top of the column is 85°. The residue is transferred to a 1-l. Claisen flask having a 30-cm. column, and is distilled under reduced pressure. Cuts are taken at 45°/20 mm., 45–64°/18 mm.,

and 64–65°/18 mm. The last fraction amounts to about 290 g. The first two fractions are redistilled and more  $\beta$ -diethylaminoethyl alcohol is obtained (Note 1). The total yield is 320–330 g. (68–70 per cent of the theoretical amount).

## 2. Notes

1. The physical properties of  $\beta$ -diethylaminoethyl alcohol are described in detail by Headlee, Collett, and Lazzell.<sup>3</sup>

## 3. Methods of Preparation

$\beta$ -Diethylaminoethyl alcohol has been prepared by reduction of diethylaminoacetic ester with sodium and alcohol,<sup>1</sup> by the action of ethylene chlorohydrin on diethylamine,<sup>2</sup> and by the action of ethylene oxide on diethylamine.<sup>3</sup>

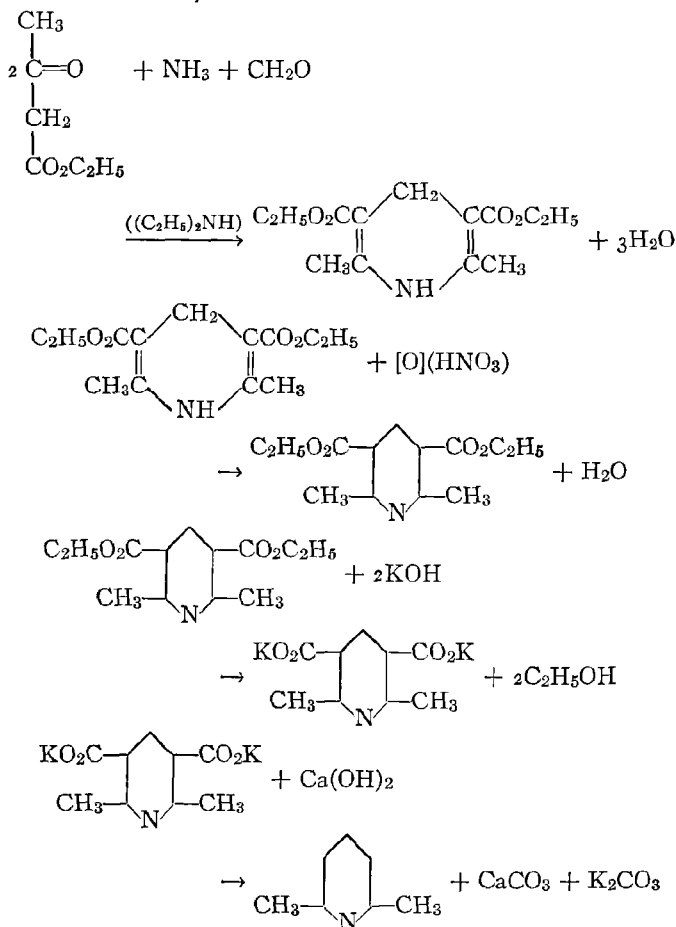
<sup>1</sup> Gault, *Compt. rend.* **145**, 126 (1907); *Bull. soc. chim.* [4] **3**, 369 (1908).

<sup>2</sup> Ladenburg, *Ber.* **14**, 1878 (1881); Soderman and Johnson, *J. Am. Chem. Soc.* **47**, 1394 (1925).

<sup>3</sup> Horne and Shriner, *J. Am. Chem. Soc.* **54**, 2928 (1932); Headlee, Collett, and Lazzell, *ibid.* **55**, 1066 (1933).

X

**2,6-DIMETHYLPYRIDINE**



Submitted by ALVIN SINGER and S. M. McELVAIN.

Checked by REYNOLD C. FUSON and CHARLES F. WOODWARD.

## 1. Procedure

To 500 g. (3.85 moles) of freshly distilled ethyl acetoacetate in a 1-l. flask set in ice and well cooled, are added 152 g. (2.0 moles) of 40 per cent aqueous formaldehyde solution and 20-25 drops of diethylamine. The flask and contents are kept cold for six hours and are then allowed to stand at room temperature for forty to forty-five hours. At the end of this time two layers are present, a lower oily layer and an upper aqueous layer. The layers are separated, and the aqueous layer is extracted with 50 cc. of ether. The ether solution is added to the oily layer, and the resulting solution is dried over 30 g. of calcium chloride. The ether is then removed by distillation on a steam bath. The residue, amounting to approximately 500 g., is diluted with an equal volume of alcohol and is thoroughly cooled in an ice bath. Ammonia is then passed into the mixture until the solution is saturated. This requires from four to eight hours, and during this time the flask is kept packed in ice. The ammoniacal alcoholic solution is allowed to stand at room temperature for forty to forty-five hours. Most of the alcohol is now evaporated; the residue is cooled, and the solid 1,4-dihydro-3,5-dicarbethoxy-2,6-dimethylpyridine is removed from the remaining alcohol on a suction filter. The dried ester melts at 175-180° and amounts to 410-435 g. (84-89 per cent of the theoretical amount).

To 200 g. (0.79 mole) of the ester in a 5-l. flask is added a mixture of 270 g. of water, 72 g. of concentrated nitric acid (sp. gr. 1.42), and 78 g. of concentrated sulfuric acid. The flask is then very cautiously heated, and the contents are kept in a swirling motion by a slow shaking of the flask by hand. The oxidation is accompanied by considerable foaming, and if the heating is too rapid, part of the reaction mixture may be lost by excessive frothing. After the foaming has subsided, the reaction mixture is again warmed cautiously until the liquid assumes a deep red color. The entire oxidation is carried out in ten to fifteen minutes. After the liquid has ceased boiling, it is treated with 500 cc. of water and 500 g. of finely chopped ice. The resulting solution is made strongly alkaline by the

gradual addition of ammonium hydroxide (sp. gr. 0.90). The precipitated 3,5-dicarbethoxy-2,6-dimethylpyridine is filtered with suction, dried on a porous plate, and then distilled (Note 1). The yield of product boiling at  $170-172^{\circ}/8$  mm. is 115-130 g., or 58-65 per cent of the theoretical amount based on the dihydro ester.

A solution of 130 g. (0.52 mole) of this ester in 400 cc. of ethyl alcohol is placed in a two-necked 2-l. flask, carrying a dropping funnel and a reflux condenser, and is heated to boiling. Then one-third of a solution (Note 2) of 78.5 g. (1.4 moles) of potassium hydroxide in 400 cc. of alcohol is added from the dropping funnel, and the alcoholic solution is boiled until it becomes clear. Then a second third of the alkali solution is added, and the reaction mixture is again boiled until any precipitate disappears. Finally, the last third of the alcoholic potassium hydroxide solution is added. The addition of the alkali requires about twenty minutes. The reaction mixture is then boiled for forty minutes longer.

The contents of the flask while still hot are poured into a 30-cm. evaporating dish and the alcohol is evaporated on a steam bath. The dry salt is pulverized and thoroughly mixed with 390 g. of calcium oxide, placed in a 2-l. copper retort (Note 3), and heated with the full flame of a Meker burner. The distillate is placed in a distilling flask and heated on a steam bath; all material distilling under  $90^{\circ}$  is removed and discarded. The residue is then allowed to stand over solid potassium hydroxide for twelve hours and is finally fractionated. The dimethylpyridine distils at  $142-144^{\circ}/743$  mm. The yield is 35-36 g. or 62-64 per cent of the theoretical amount based on the 3,5-dicarbethoxy-2,6-dimethylpyridine, or 30-36 per cent based on the original ethyl acetoacetate.

## 2. Notes

1. Before the diminished pressure is applied, the 3,5-dicarbethoxy-2,6-dimethylpyridine should be melted by immersing the distilling flask in boiling water. If this is not done, considerable foaming takes place during the distillation.

2. If the entire amount of alcoholic potassium hydroxide solution is added at this point, there is precipitated a colorless solid, which does not dissolve even on prolonged heating.

3. It is very desirable that a metal retort be used for this decomposition since glass flasks soften at the temperature necessary for the reaction.

### 3. Methods of Preparation

2,6-Dimethylpyridine has been isolated from the basic fraction of coal tar<sup>1</sup> and also from the bone oil fraction distilling at 139–142°.<sup>2</sup> It has also been prepared from ethyl aceto-pyruvate and ethyl  $\beta$ -aminocrotonate.<sup>3</sup>

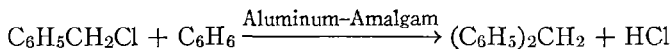
<sup>1</sup> Lunge and Rosenberg, Ber. **20**, 129 (1887); Heap, Jones, and Speakman, J. Am. Chem. Soc. **43**, 1936 (1921); Komatsu and Mohri, J. Chem. Soc. Japan **52**, 722 (1931) [C. A. **26**, 4936 (1932)].

<sup>2</sup> Ladenberg and Roth, Ber. **18**, 51 (1885).

<sup>3</sup> Mumm and Huneke, Ber. **50**, 1568 (1927).

## XI

### DIPHENYLMETHANE



Submitted by W. W. HARTMAN and ROSS PHILLIPS.

Checked by REYNOLD C. FUSON and S. H. BABCOCK.

#### 1. Procedure

IN a 5-l. flask provided with a reflux condenser and an S-tube attached to a dropping funnel, are placed 2000 g. (2300 cc., 25.6 moles) of benzene, which has been dried by distilling until the distillate comes over clear, and 10 g. of amalgamated aluminum turnings (Note 1). The benzene is heated to boiling on a steam bath, the steam is turned off, and 500 g. (3.96 moles) of benzyl chloride is added at such a rate as to cause the solution to boil (Note 2). The hydrogen chloride is absorbed in water (see p. 2) or allowed to pass out-of-doors. When all the benzyl chloride has been added (one hour), the mixture is warmed for ten to fifteen minutes or until the evolution of hydrogen chloride ceases. When cool, the benzene solution of diphenylmethane is decanted from the small amount of tarry material (Note 3) and washed with 5 per cent sodium hydroxide solution and then with water. After a partial drying with calcium chloride, the benzene is distilled from a steam bath and the residue fractionated under diminished pressure. The forerun is collected up to 125°/10 mm., the main product at 125-130°/10 mm., and an after-run up to 150°/10 mm. (Note 4). Redistillation of the forerun and after-run yields a small amount of material which is added to the main fraction. The latter is chilled and a small amount of oil is decanted from the crystals. The yield of material melting at 24-25° is 330-350 g. (49.5-52.5 per cent of the theoretical amount).

#### 2. Notes

1. Amalgamated aluminum is prepared as follows: Aluminum turnings, freed from any oil by washing with ether, are stirred

with a 5 per cent mercuric chloride solution for a few minutes and then washed quickly with water followed by methyl alcohol. The amalgamated aluminum is used at once.

2. At times the reaction is slow in starting. Not more than 50-60 g. of benzyl chloride is added at first, and the mixture is heated until the evolution of hydrochloric acid indicates that the reaction is under way. If too much benzyl chloride is present when the reaction starts, the contents of the flask may boil over.

3. Succeeding batches may be started in the same flask containing the aluminum turnings and the trace of tarry material without the addition of further catalyst; these batches do not show any signs of an induction period.

4. The material in the residue and high-boiling fraction may partially be converted into diphenylmethane by heating with one-third its weight of aluminum chloride and five times its weight of benzene.

### 3. Methods of Preparation

Diphenylmethane has been prepared with aluminum chloride as a catalyst from methylene chloride and benzene,<sup>1</sup> from chloroform and benzene as a by-product in the preparation of triphenylmethane,<sup>2</sup> and from benzyl chloride and benzene.<sup>3</sup> It has been prepared by the reduction of benzophenone with hydriodic acid and phosphorus,<sup>4</sup> or with sodium and alcohol.<sup>5</sup> It has also been made by heating a solution of benzyl chloride in benzene with zinc dust,<sup>6</sup> or with zinc chloride.<sup>7</sup> The above method is only a slight modification of the original method of Hirst and Cohen.<sup>8</sup>

<sup>1</sup> Friedel and Crafts, *Bull. soc. chim.* [2] **41**, 324 (1884); Schwarz, *Ber.* **14**, 152<sup>b</sup> (1881).

<sup>2</sup> E. Fischer and O. Fischer, *Ann.* **194**, 253 (1878); Böeseken, *Rec. trav. chim.* **22**, 307 (1903); Friedel and Crafts, *Ann. chim. phys.* [6] **1**, 490 (1884).

<sup>3</sup> Friedel and Balsohn, *Bull. soc. chim.* [2] **33**, 337 (1880).

<sup>4</sup> Graebe, *Ber.* **7**, 1624 (1874).

<sup>5</sup> Klages and Altendorf, *ibid.* **31**, 999 (1898).

<sup>6</sup> Zincke, *Ann.* **159**, 374 (1871).

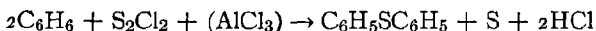
<sup>7</sup> Friedel and Crafts, *Ann. chim. phys.* [6] **1**, 478 (1884).

<sup>8</sup> Hirst and Cohen, *J. Chem. Soc.* **67**, 827 (1895).



## XII

### DIPHENYL SULFIDE



Submitted by W. W. HARTMAN, L. A. SMITH and J. B. DICKEY.

Checked by REYNOLD C. FUSON and S. H. BABCOCK.

#### 1. Procedure

IN a 5-l. three-necked, round-bottomed flask fitted with a mechanical stirrer, dropping funnel, and a condenser connected to an apparatus for removing hydrogen chloride (see p. 2), are placed 858 g. (980 cc., 11 moles) of dry benzene (Note 1) and 464 g. (3.48 moles) of aluminum chloride. The reaction mixture is cooled in an ice bath to 10° and then 405.1 g. (3 moles) of commercial sulfur chloride in 390 g. (450 cc., 5 moles) of benzene is added, with stirring, over a period of one hour, the temperature being kept at about 10°. The reaction begins at once as evidenced by the evolution of hydrogen chloride and the separation of a yellow viscous aluminum chloride complex. When all of the sulfur chloride has been added, the reaction mixture is removed from the ice bath, stirred at room temperature for two hours, and then heated at 30° until practically no hydrogen chloride is evolved (one hour). The mixture is then poured on 1 kg. of cracked ice, and, when hydrolysis is complete, the benzene layer is separated from the water layer by means of a separatory funnel. The benzene is distilled on a steam bath, and the resulting dark-colored oil is cooled to 0° and filtered through a Büchner funnel to remove the sulfur which separates. The residue is dissolved in 500 cc. of commercial methyl alcohol and the solution is cooled to 0°. Stirring is continued for three hours and the precipitated sulfur is removed as before. The alcohol is removed on a steam bath and the residue

is distilled from a 1-l. modified Claisen flask with a water-cooled side arm receiver. After a small amount of low-boiling product passes over, there is obtained 470-490 g. (Note 2) of a yellow liquid boiling at 155-170°/18 mm. The material thus obtained is heated for one hour on a steam bath, with stirring, with 70 g. of zinc dust and 200 g. of 40 per cent sodium hydroxide solution (Note 3). The diphenyl sulfide is then separated from the sodium hydroxide, washed with two 500-cc. portions of water, dried over anhydrous sodium sulfate, and distilled. The yield of colorless diphenyl sulfide boiling at 162-163°/18 mm. is 450-464 g. (81-83 per cent of the theoretical amount).

## 2. Notes

1. The benzene can be dried by distilling on a steam bath until the distillate is no longer milky. About 15 per cent of the benzene is distilled.

2. On distillation of the residue in the distillation flask there is obtained a fraction boiling at 170-200°/18 mm. Crystallization of this material from methyl alcohol yields 8-10 g. of thianthrene, melting at 155-156°.

3. It is necessary to treat the diphenyl sulfide as described in order to obtain a colorless product.

## 3. Methods of Preparation

Diphenyl sulfide can best be prepared by treating benzene and aluminum chloride with sulfur chloride,<sup>1</sup> sulfur dichloride,<sup>2</sup> or sulfur.<sup>3</sup> In addition to diphenyl sulfide there are found traces of thiophenol and varying amounts of thianthrene.

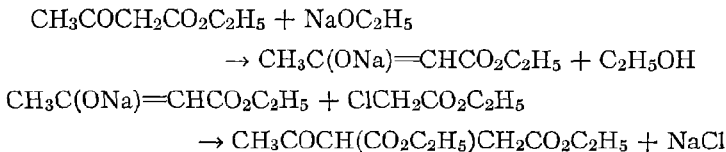
<sup>1</sup> Böeseken, *Rec. trav. chim.* **24**, 209 (1905); Böeseken and Watermann, *ibid.* **29**, 319 (1910); Böeseken and Koning, *ibid.* **30**, 116 (1911); Genveresse, *Bull. soc. chim.* [3] **15**, 409 (1896); Hartman, Smith and Dickey, *Ind. Eng. Chem.* **24**, 1317 (1932).

<sup>2</sup> Böeseken, *Rec. trav. chim.* **24**, 217 (1905); Böeseken and Koning, *ibid.* **30**, 116 (1911).

<sup>3</sup> Friedel and Crafts, *Ann. chim. phys.* [6] **14**, 437 (1888); Böeseken, *Rec. trav. chim.* **24**, 17, 219 (1905).

### XIII

#### ETHYL ACETOSUCCINATE



Submitted by HOMER ADKINS, NEVILLE ISBELL, and BRUNO WOJCIK.

Checked by JOHN R. JOHNSON and H. R. SNYDER.

#### 1. Procedure

IN a 3-l. three-necked, round-bottomed flask fitted with a mechanical stirrer, reflux condenser, and separatory funnel is placed 400 cc. of absolute alcohol (Note 1). Through the condenser tube is added slowly, 23 g. (1 gram atom) of clean sodium cut into thin slices. The completion of the reaction is hastened by heating the flask on a steam bath. When the sodium has dissolved completely, 143 g. (1.1 moles) of ethyl acetoacetate is introduced slowly. After starting the mechanical stirrer, 123 g. (1 mole) of ethyl chloroacetate (Note 2) is added slowly over a period of an hour, and the reaction mixture is refluxed for five to six hours. At this point the reaction mixture should no longer give an alkaline reaction with moist litmus.

After cooling, the precipitated sodium chloride is removed by filtering with suction and is washed with two 50-cc. portions of absolute alcohol. The alcohol is removed by distilling through a short column from a steam bath. The residue is filtered and transferred to a round-bottomed flask and is fractionated under reduced pressure through a Widmer column containing an 8-cm. spiral (Note 3). The fraction boiling at 121–124°/5 mm. is collected. The yield is 121–134 g. (56–62 per cent of the theoretical amount) (Note 4).

## 2. Notes

1. A good grade of absolute alcohol is required. For this purpose ordinary absolute alcohol may be dried by treating with a little sodium, adding a few cubic centimeters of ethyl succinate, and distilling directly into the reaction flask (see also Org. Syn. Coll. Vol. 1, 255).

2. Ethyl chloroacetate boiling at 142–145° was used. This ester can be prepared readily by refluxing for six hours a mixture of 200 g. of chloroacetic acid, 120 g. of absolute alcohol, and 25 g. of concentrated sulfuric acid.<sup>1</sup> The product is purified in the conventional way, and the yield is 185 g. (70 per cent of the theoretical amount).

3. It is advantageous to use an electrically heated column for this fractionation. The principal by-product of the reaction is ethyl  $\beta$ -acetotricarballylate<sup>2</sup> (b.p. 190°/16 mm.), formed by further action of ethyl chloroacetate upon the initial product.

4. Ethyl  $\alpha$ -acetoglutarate may be prepared in a similar way by using 181 g. (1 mole) of ethyl  $\alpha$ -bromopropionate (Org. Syn. Coll. Vol. 1, 241) instead of ethyl chloroacetate. The product in this case is collected at 132–134°/4 mm. and weighs 120 g. (52 per cent of the theoretical amount).

## 3. Methods of Preparation

Ethyl acetosuccinate has been prepared by the interaction of ethyl sodio-acetoacetate and ethyl chloroacetate<sup>1</sup> or bromoacetate.<sup>2</sup> The method given above is a modification<sup>3</sup> of that given by Conrad.<sup>1</sup>

<sup>1</sup> Conrad, Ann. **188**, 218 (1877).

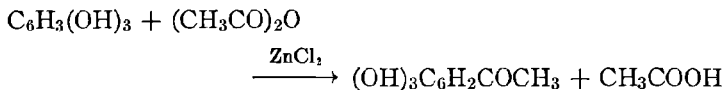
<sup>2</sup> Emery, Ber. **23**, 3755 (1890); Fichter and Pfister, *ibid.* **37**, 1997 (1904).

<sup>3</sup> Isbell, Wojcik and Adkins, J. Am. Chem. Soc. **54**, 3685 (1932).

## XIV

### GALLACETOPHENONE

#### (2,3,4-Trihydroxyacetophenone)



Submitted by I. C. BADHWAR and K. VENKATARAMAN.  
Checked by W. W. HARTMAN and L. J. ROLL.

#### 1. Procedure

IN a 250-cc. round-bottomed flask fitted with a reflux condenser to which is attached a calcium chloride tube, 28 g. (0.21 mole) of freshly fused and finely powdered zinc chloride (Note 1) is dissolved in 40 g. (38 cc.) of glacial acetic acid by heating in an oil bath at 135–140°. Forty grams (0.37 mole) of 95 per cent acetic anhydride is then added to the clear, pale brown liquid, followed by the addition in one lot of 50 g. (0.4 mole) of distilled pyrogallol (Note 2). The mixture is heated at 140–145° (Note 3) for forty-five minutes with frequent and vigorous shaking. The unused acetic anhydride and acetic acid are removed by distilling under reduced pressure. The red-brown cake is broken up by the addition of 300 cc. of water with mechanical stirring for a few minutes. The mixture is cooled in ice water, filtered with suction, and washed with cold water. The crude material, 45–50 g., is crystallized from 500 cc. of boiling water saturated with sulfur dioxide. The yield of straw-colored needles melting at 171–172° is 36–38 g. (54–57 per cent of the theoretical amount). On saturating the mother liquor with salt and cooling to 10°, 4–5 g. of crude material is obtained, which on recrystallization yields 3–4 g. of pure material.

## 2. Notes

1. A good quality of zinc chloride must be used, and it is an advantage to fuse it immediately before use.

2. Variations in the proportions of acetic acid, anhydride, and zinc chloride did not result in increased yields.

3. The temperature must be carefully regulated, and in no case must it exceed  $150^{\circ}$ . In this preparation, as well as in the preparation of other ketones by the Nencki reaction, higher temperatures lead to the formation of a highly colored and resinous product which probably contains a little diketone.

4. This method has been used for the preparation of other phenolic ketones such as resacetophenone, 2-acetyl-1-naphthol,<sup>1</sup> 2-phenylacetyl-1-naphthol and 2-phenylpropionyl-1-naphthol.<sup>2</sup>

## 3. Methods of Preparation

The method described above is a modification of the process of Nencki and Sieber.<sup>3</sup> Gallacetophenone has also been prepared by treating pyrogallol with acetyl chloride.<sup>4</sup>

<sup>1</sup> Witt and Braun, Ber. **47**, 3227 (1914).

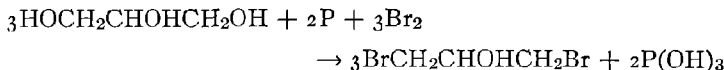
<sup>2</sup> Cheema and Venkataraman, J. Chem. Soc. **1932**, 919.

<sup>3</sup> Nencki and Sieber, J. pr. Chem. [2] **23**, 151, 538 (1881); Nencki, Ber. **27**, 2737 (1884). See also Crabtree and Robinson, J. Chem. Soc. **121**, 1038 (1922).

<sup>4</sup> Einhorn and Hollandt, Ann. **301**, 107 (1898); Fischer, Ber. **42**, 1020 (1909).

## XV

### GLYCEROL $\alpha,\gamma$ -DIBROMOHYDRIN



Submitted by GÉZA BRAUN.

Checked by R. C. FUSON and S. H. BABCOCK.

#### 1. Procedure

IN a 3-l. three-necked, round-bottomed flask fitted with a powerful glycerol-sealed stirrer, a dropping funnel, and an outlet tube for escaping gases, 1600 g. (17.4 moles) of glycerol is thoroughly mixed with 200 g. (6.5 gram atoms) of red phosphorus (Note 1). Nine hundred cubic centimeters (2808 g., 17.5 moles) of bromine (Note 2) is then gradually added, with effective stirring (Note 3), through the dropping funnel in the course of about eight hours. To minimize the escape of bromine, the end of the dropping funnel should almost reach the bottom of the flask. The by-product gases, consisting mainly of hydrogen bromide and some bromine, are led over concentrated sodium hydroxide solution or to a gas trap (see p. 2). The reaction is exothermic, and the temperature quickly rises to 80–100°; then the addition of bromine is so regulated that the temperature of the mixture is maintained at this point. Toward the end of the period of addition of bromine, the flask is placed in a water bath at 70–75°. After all the bromine has been added, the mixture is allowed to stand overnight and is then warmed on the water bath until all the bromine is consumed (one to two hours). Then the reaction mixture is transferred to a 3-l. round-bottomed flask, provided with a two-holed rubber stopper carrying a wide delivery tube, a capillary tube and an oil bath, and is distilled under reduced pressure with a water pump. The receiver is cooled with water.

At first a mixture of hydrobromic acid and water passes over; later the dibromohydrin distills. The temperature of the bath is raised as fast as the boiling of the mass permits, being eventually brought to  $180^{\circ}$ . The distillation is carefully watched at the end and immediately interrupted at the first sign of decomposition. This is clearly indicated by gas formation, in consequence of which the vacuum cannot be maintained at the previous level. To the straw-yellow distillate a slight excess of solid sodium bicarbonate is added with continuous shaking until effervescence ceases. The inorganic salts are removed by filtration, and the aqueous layer of the filtrate is separated from the crude dibromohydrin. The latter is purified by fractional distillation under reduced pressure from a 2-l. Claisen flask. The distillation is continued until no more water passes over and the inside temperature reaches  $100^{\circ}$ . Then the dibromohydrin is separated from the water in the distillate, dried with anhydrous sodium sulfate, filtered, and poured back into the distilling flask. By this operation the water is largely removed (Note 4). Then the distillation is continued as before, and after a small forerun the dibromohydrin boils at  $110-112^{\circ}$  under 20 mm. pressure (Note 5). The yield is 2000-2050 g. (52-54 per cent of the theoretical amount) of a colorless product.

The dibromohydrin is a heavy, colorless liquid with a characteristic odor. On standing it gradually becomes yellow. Its specific gravity at  $20^{\circ}$  is about 2.14.

## 2. Notes

1. The red phosphorus should be thoroughly mixed with the glycerol before the addition of the bromine. The bromine should not come into contact with the dry phosphorus or a violent reaction will occur.

2. Commercial 98 per cent glycerol and U.S.P. bromine may be used in the preparation.

3. A powerful stirrer is necessary because of the viscous nature of the reaction mixture.

4. The water derives from the chemical interaction of phos-



phorous acid with the glycerol or with the bromohydrins. Better yields are obtained when the theoretical amount of bromine is used, although on account of this secondary reaction a less amount should suffice.

5. The crude dibromohydrin distils without any decomposition at 10–15 mm. pressure if the temperature of the oil bath is not raised over 190°. Above this temperature formation of acrolein derivatives begins, which, even if present in very small amounts, makes the dibromohydrin lachrymatory.

### 3. Methods of Preparation

Glycerol  $\alpha,\gamma$ -dibromohydrin has been prepared from glycerol and phosphorus tribromide;<sup>1</sup> from glycerol and bromine;<sup>2</sup> from glycerol, red phosphorus, and bromine.<sup>3,4,5</sup>

<sup>1</sup> Berthelot <sup>et</sup> Luca, Ann. chim. phys. [3], 48, 306 (1856).

<sup>2</sup> Barth, Ann. 124 349 (1862).

<sup>3</sup> Aschan, Ber. 23, 1826 (1890).

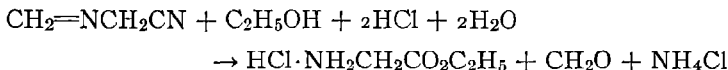
<sup>4</sup> Lespieau, Ann. chim. phys. [7] 11, 236 (1897).

<sup>5</sup> Géza Braun, J. Am. Chem. Soc. 52, 3172 (1930).



## XVI

### GLYCINE ETHYL ESTER HYDROCHLORIDE



Submitted by C. S. MARVEL.

Checked by L. F. FIESER and S. L. JUDKINS.

#### 1. Procedure

In a 3-l. round-bottomed flask are placed 500 cc. (400 g., 8.7 moles) of absolute alcohol which has been saturated in the cold with hydrochloric acid gas (Note 1), 870 cc. (680 g., 20 moles) of 96 per cent alcohol (Note 2) and 70 g. (1.03 moles) of methyleneaminoacetonitrile (Note 3). This mixture is refluxed on a steam bath for three hours (Note 4). During the refluxing, ammonium chloride separates. After the reaction is complete, the hot alcohol solution is filtered with suction and the filtrate cooled, thus allowing the glycine ester hydrochloride to separate out in fine white needles. The product is filtered with suction, sucked as dry as possible on the filter, and then allowed to dry in the air. The yield is about 110 g. The alcohol from the filtrate is distilled (Note 5) until about one-third of its volume is left and again cooled and a second crop of crystals is obtained. The total yield of product, m.p. 142-143°, varies from 125 to 129 g. (89-91 per cent of the theoretical amount). If a very pure product is desired, it may be recrystallized from absolute alcohol.

#### 2. Notes

1. The 500 cc. of absolute alcohol is cooled in an ice bath and treated with dry hydrogen chloride until 163 g. has been added, an amount sufficient for saturation. The solution should be protected from the moisture of the air with a calcium chloride tube.

2. It is important to use the strengths of alcohol specified in the directions if the best yields are to be obtained, and it is advisable to test the alcohol with a hydrometer just before using. The 870 cc. of 96 per cent alcohol contains just enough water for the hydrolysis. If, therefore, a less concentrated alcohol is used, the glycine ester hydrochloride does not form so readily and does not separate as easily from solution. Experiments using 96 per cent alcohol saturated with hydrochloric acid and 870 cc. of 96 per cent alcohol gave a yield of product lower by 8 to 10 g. A more dilute alcohol than 96 per cent gives a much poorer grade and yield of the glycine ester hydrochloride.

3. The crude material as described in *Org. Syn. Coll. Vol. 1*, 347, is satisfactory.

4. A cork and not a rubber stopper should be used during the refluxing, as rubber stoppers will cause the product to be colored.

5. Care must be taken that no water gets into the alcohol, as glycine ester hydrochloride is quite soluble in water. Concentration of the filtrate on the steam bath should not be carried out in an open vessel because the solution will take up moisture and the product will not crystallize.

### 3. Methods of Preparation

Glycine ethyl ester hydrochloride has been prepared by the action of absolute alcohol and hydrogen chloride on glycine;<sup>1</sup> from glycylic chloride and alcohol;<sup>2</sup> by the action of ammonia<sup>3</sup> or hexamethylenetetramine<sup>4</sup> on chloroacetic acid, and subsequent hydrolysis with alcoholic hydrochloric acid; and by the action of hydrogen chloride and alcohol on methyleneaminoacetonitrile.<sup>5</sup>

<sup>1</sup> Curtius and Göbel, *J. prakt. Chem.* [2] **37**, 159 (1888); Harries and Weiss, *Ann.* **327**, 365 (1903).

<sup>2</sup> E. Fischer, *Ber.* **38**, 2916 (1905).

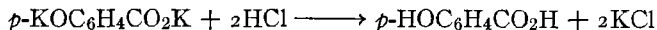
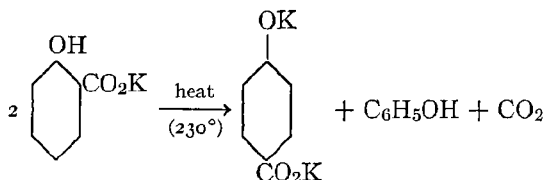
<sup>3</sup> Hantzsch and Silberrad, *ibid.* **33**, 70 (1900); Hantzsch and Metcalf, *ibid.* **29**, 1681 (1896).

<sup>4</sup> Auger, *Bull. soc. chim.* [3] **21**, 6 (1899); Locquin, *ibid.* **23**, 662 (1900).

<sup>5</sup> Jay and Curtius, *Ber.* **27**, 60 (1894); Klages, *ibid.* **36**, 1508 (1902).

## XVII

### *p*-HYDROXYBENZOIC ACID



Submitted by C. A. BUEHLER and W. E. CATE.

Checked by JOHN R. JOHNSON and C. P. NICHOLS.

#### 1. Procedure

SIXTY grams (0.43 mole) of potassium carbonate (Note 1) is slowly stirred into a mixture of 100 g. (0.725 mole) of salicylic acid (U.S.P.) and 150 cc. of water contained in a 20-cm. porcelain dish. The solution is evaporated on a steam bath until a thick, pasty residue is obtained. This is broken up into small pieces and dried in an oven at 105–110° for two hours. The solid is then ground as finely as possible, dried for another two hours at 105–110°, and again ground to a fine powder.

The finely powdered mixture of potassium salicylate and carbonate is placed in a 500-cc. round-bottomed flask which is immersed in an oil bath so that only a small portion of the neck protrudes from the bath (Note 2). The bath is heated to 240° (Note 3) and maintained at this temperature for one and one-half hours. During this time the solid in the flask is stirred occasionally with a curved glass rod flattened at the end.

When the reaction is completed (Note 4), the product is transferred as completely as possible, while hot, into a 2-l. flask containing 1 l. of hot water. The reaction flask is rinsed with

several portions of the hot solution. The alkaline solution is acidified with concentrated hydrochloric acid (about 75 cc. is required), heated nearly to boiling, and treated with 5-6 g. of decolorizing charcoal. The hot solution is filtered to remove a small quantity of brown resin. The filtrate is cooled under the tap, and the crude brown crystalline product is filtered with suction. The filtrate is concentrated to a volume of approximately 300 cc. and cooled as before. The second crop of the crude acid is filtered with suction and combined with the main portion. The total weight of crude *p*-hydroxybenzoic acid, m.p. 208-211°, is 40-45 g.

The crude acid is dissolved in 300 cc. of hot water, boiled with 4-5 g. of decolorizing charcoal for a few minutes, and the solution filtered. After cooling thoroughly under the tap the purified product is filtered with suction and washed with 10-15 cc. of cold water. The purified acid weighs 35-40 g. (70-80 per cent of the theoretical amount) and melts at 211-212°.

## 2. Notes

1. An excess of potassium carbonate is used since it prevents the mass from caking during the subsequent heating. Although the original mixture is strongly alkaline a clear solution may not be obtained until the dish is heated.

2. In this way the phenol formed in the reaction is allowed to distil out of the mixture. This operation should be carried out in a hood.

3. The temperature reported is that of the oil bath; the internal temperature is approximately 230°. The temperature should be controlled carefully since pronounced decomposition sets in at higher temperatures.

4. The completeness of the reaction may be determined roughly by treating a small test portion with 3-4 cc. of hot water and acidifying with concentrated hydrochloric acid. Since *p*-hydroxybenzoic acid is relatively soluble and salicylic acid only sparingly so, the absence of a precipitate in the warm solution indicates that the reaction is essentially complete.

### 3. Methods of Preparation

*p*-Hydroxybenzoic acid has been prepared by heating potassium phenoxide in a stream of carbon dioxide<sup>1</sup> or with carbon tetrachloride,<sup>2</sup> and by heating *p*-cresol with alkalies and various metallic oxides.<sup>3</sup> The procedure described above is similar to one which appears in the early literature.<sup>4</sup>

<sup>1</sup> Kolbe, J. prakt. Chem. [2] **10**, 100 (1874); Hartmann, *ibid.* [2] **16**, 39 (1877); Ost, *ibid.* [2] **20**, 208 (1879).

<sup>2</sup> Reimer and Tiemann, Ber. **9**, 1285 (1876); Hasse, *ibid.* **10**, 2186 (1877).

<sup>3</sup> Graebe and Kraft, Ber. **39**, 797 (1906); Friedländer and Löw-Beer, ~~Ger. pat.~~ 170,230 [Frdl. **8**, 158 (1906)].

<sup>4</sup> Kolbe, J. prakt. Chem. [2] **11**, 24 (1875); Heyden, ~~Ger. pat.~~ 48,356 [Frdl. **2**, 132 (1888)].

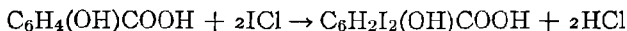




## XVIII

### 2-HYDROXY-3,5-DIODOBENZOIC ACID

#### (Diiodosalicylic Acid)



Submitted by G. H. WOOLLETT, and W. W. JOHNSON.

Checked by W. W. HARTMAN and E. J. RAHRS.

#### 1. Procedure

TWENTY-FIVE grams (0.18 mole) of salicylic acid (m.p. 159–160°) is dissolved (Note 1) in 225 cc. of glacial acetic acid in a 2-l. beaker provided with a mechanical stirrer. To this is added with stirring a solution of 62 g. (0.38 mole) of iodine chloride (Note 2) in 165 cc. of glacial acetic acid, and then 725 cc. of water is added. A yellow precipitate of diiodosalicylic acid appears. The reaction mixture is gradually heated with stirring on a hot plate to 80° and kept at approximately that temperature for twenty minutes. The entire period of heating should be about forty minutes. Toward the end of the reaction the mixture becomes rather difficult to stir because of the voluminous precipitate. After cooling to room temperature (Note 3), the precipitate is filtered on a Büchner funnel and washed with acetic acid and then with water. When no more water is removed by suction, the solid (75 g.) is dissolved in 100 cc. of warm acetone and filtered by gravity. To the filtrate 400 cc. of water is slowly added with shaking. The fine, flocculent precipitate is filtered by suction, washed with water, and dried. The yield of diiodosalicylic acid melting at 235–236° is 64–64.5 g. (91–92 per cent of the theoretical amount). (Note 4).

#### 2. Notes

1. The amount of glacial acetic acid used may not be sufficient to dissolve completely the salicylic acid. Solution will

be completed upon the addition of the iodine chloride solution.

2. Iodine chloride of sufficient purity for this preparation may be made as follows: Dry chlorine is passed into 127 g. of iodine contained in a 125-cc. distilling flask until the weight has increased 34.5 g. The chlorine should be led in at or below the surface of the iodine while the flask is gently agitated. An excess of iodine is essential. When the above weight increase has been obtained, the iodine chloride is distilled in an ordinary distilling apparatus, the receiver of which is a filtering flask protected from atmospheric moisture by a calcium chloride tube. The fraction boiling between  $97^{\circ}$  and  $105^{\circ}$  is collected. Yield, 142 g. (87 per cent). The iodine chloride may be preserved in a dry, glass-stoppered bottle.

3. Free iodine, if present, is removed by the addition of 5 per cent sodium sulfite solution.

4. The checkers found that 4-hydroxy-3,5-diiodobenzoic acid may be made from 4-hydroxybenzoic acid using the above directions with the exception that the product is not recrystallized from acetone, in which it is only slightly soluble. The yield of 4-hydroxy-3,5-diiodobenzoic acid melting at  $278-279^{\circ}$  with decomposition is 59 g. (84 per cent of the theoretical amount).

### 3. Methods of Preparation

The method given is based on that of Victor Cofman.<sup>1</sup> Diiodosalicylic acid has been prepared by heating salicylic acid with iodine in alcohol;<sup>2</sup> by using the same reagents with addition of mercuric oxide;<sup>3</sup> by treating salicylic acid with iodine in the presence of alkali;<sup>3,4</sup> and by treating salicylic acid with iodine and iodic acid.<sup>5</sup> None of these methods, however, appears to give a good yield or a pure product.

<sup>1</sup> Cofman, Gazz. chim. ital. **50**, II, 297 (1920).

<sup>2</sup> Lauteman, Ann. **120**, 300 (1861).

<sup>3</sup> Weselsky, ibid. **174**, 103 (1874).

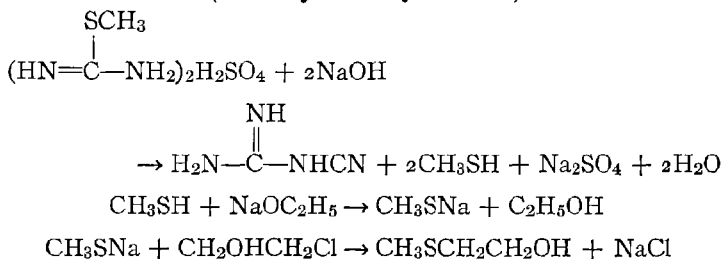
<sup>4</sup> Kekulé, ibid. **131**, 226 (1864).

<sup>5</sup> Liechti, ibid. Spl. **7**, 133, 141 (1872).

## XIX

### β-HYDROXYETHYL METHYL SULFIDE

(S-Methylthiolethyl Alcohol)



Submitted by WALLACE WINDUS and P. R. SHILDNECK.

Checked by H. T. CLARKE and S. GURIN.

### 1. Procedure

IN a 2-l. three-necked flask, fitted with a dropping funnel, a stopcock, and a long condenser, is placed 556 g. (2 moles) (Note 1) of methyl isothioureia sulfate (Org. Syn. 12, 52). From the end of the condenser the gas is led into a safety trap, consisting of an empty gas-washing bottle, which in turn is connected to a second wash bottle containing 100 cc. of dilute sulfuric acid (1 volume of concentrated sulfuric acid to 2 volumes of water). The gas is then passed through a tower (height about 30 cm.) containing calcium chloride into an empty 2-l. flask, which acts as a trap, and finally into a 2-l. flask containing the absorption mixture. This consists of 80.5 g. (3.5 gram atoms) of clean sodium dissolved in 1500 cc. of absolute alcohol. The exit tube from the absorption mixture is attached to an empty 1-l. flask and this is connected with a 1-l. flask containing 500 cc. of a saturated solution of lead acetate (Note 2). The exit tube from the latter leads to a suction pump. A very slow current of air is drawn through the apparatus while 800 cc. of cold 5 N

sodium hydroxide is added to the methyl isothioureia sulfate through the dropping funnel. The mixture is warmed very slowly to generate the methyl mercaptan (Note 3). As the reaction nears completion (after about two hours), the mixture is heated strongly for about thirty minutes (Note 4).

The solution of sodium methyl sulfide in absolute alcohol is transferred to a 3-l. three-necked flask, which is placed on a steam bath and fitted with a dropping funnel, a reflux condenser, and a mechanical stirrer. The solution is heated until the alcohol begins to boil. Heating is then discontinued and 302 g. (3.75 moles) of ethylene chlorohydrin (Note 5) is added dropwise with efficient stirring over a period of about two hours (Note 6). The reaction mixture is concentrated by distilling as much of the alcohol as possible on the steam bath. The mixture is then allowed to cool and the sodium chloride removed by filtration. The flask is rinsed, and the sodium chloride washed with three 100-cc. portions of 95 per cent alcohol. The combined filtrate and washings are concentrated on the steam bath under reduced pressure until no further distillate passes over. The residue is then transferred to a modified Claisen flask (Org. Syn. Coll. Vol. 1, 125) and fractionally distilled under reduced pressure. The yield is 238-265 g. (74-82 per cent of the theoretical amount based on the sodium used) of a product boiling at 68-70°/20 mm.

## 2. Notes

1. Quantities of material five times as large as the above may be used without decreasing the yield of product. In such cases it is more convenient to filter the sodium chloride before concentrating the solution.

2. The lead acetate removes any unreacted methyl mercaptan by precipitating it as the lead salt.

3. The rate of heating controls the rate of evolution of the methyl mercaptan. After the rapid evolution of the gas begins, the reaction mixture should be heated very gently. A slight suction aids in obtaining a regular flow of the gas.

4. The evolution of methyl mercaptan is almost complete

after one and one-half to two hours. Prolonged vigorous heating increases the amount of ammonia evolved.

5. The ethylene chlorohydrin should be redistilled and the fraction boiling at 126–128° should be used.

6. The reaction is usually complete immediately after the addition of the ethylene chlorohydrin, obviating the necessity for refluxing the mixture. The reaction is complete when the solution is neutral to litmus paper.

### 3. Methods of Preparation

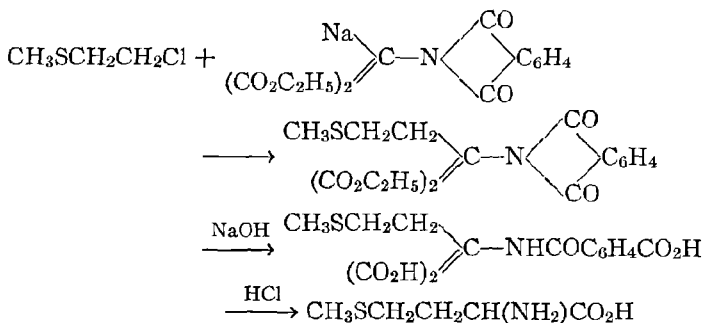
The methods for preparing methyl mercaptan and  $\beta$ -hydroxyethyl methyl sulfide are essentially those of Arndt<sup>1</sup> and Kirner,<sup>2</sup> respectively.

<sup>1</sup> Arndt, Ber. **54**, 2238 (1921).

<sup>2</sup> Kirner, J. Am. Chem. Soc. **50**, 2451 (1928).



## XX

**dl-METHIONINE**

Submitted by G. BARGER and T. E. WEICHELBAUM.

Checked by H. T. CLARKE and S. GURIN.

**1. Procedure**

*A. Ethyl Sodium Phthalimidomalonate.*—To a solution of 9.2 g. (0.4 gram atom) of sodium in 300 cc. of absolute alcohol at 60° is added, with efficient stirring, 126 g. (0.41 mole) of ethyl phthalimidomalonate (Org. Syn. Coll. Vol. 1, 266). The mixture is rapidly chilled to 0° and the crystalline product filtered at once by suction and washed successively with two 200-cc. portions of absolute alcohol and two 200-cc. portions of ether. After first drying in a vacuum desiccator and then heating for eight hours under 15 mm. pressure in a flask suspended in an oil bath at 145–155° (Note 1), it weighs 108–111 g. (82–85 per cent of the theoretical amount).

*B. Ethyl 1-Methylthiol-3-phthalimidopropane-3,3-dicarboxylate.*—A mixture of 85 g. (0.26 mole) of ethyl sodium phthalimidomalonate and 43 g. (0.39 mole) of β-chloroethyl methyl sulfide (p. 18) is heated in an oil bath at 160–165° in a 1-l. three-necked flask, fitted with a condenser, a thermometer, and a stoppered

glass tube for sampling. After one and a half to two hours the mixture is no longer alkaline to litmus. The excess chloroethyl methyl sulfide is distilled under reduced pressure (Note 2), the residual oil is treated with 150 cc. of warm water, and the resulting mixture is transferred to a beaker and chilled. The crystalline material is filtered by suction, washed with 100 cc. of cold water, and recrystallized from the smallest possible quantity of warm absolute alcohol. In this way 75–79 g. (76–81 per cent of the theoretical amount) of a pure product, melting at 66–67°, is obtained.

*C. 1-Methylthiol-3-phthalamidopropane-3,3-dicarboxylic Acid.*—A solution of 25 g. (0.066 mole) of the above ester in 30 cc. of 95 per cent alcohol is heated on the steam bath in a 200-cc. round-bottomed flask, and 70 cc. of 5 *N* sodium hydroxide is added. The cloudy liquid is heated until a sample gives a clear solution on dilution with water; this occurs after about two hours. The solution is then chilled to 0° and cautiously neutralized to congo red with 0.2 *N* hydrochloric acid, whereupon 75 cc. of 5 *N* hydrochloric acid is slowly added, the temperature being maintained at 0°. The acid separates as colorless crystals. This separation is completed by the slow addition of 60 cc. of concentrated hydrochloric acid (sp. gr. 1.19). The product is filtered by suction and washed free of salt with small quantities of ice-cold water. After drying *in vacuo*, the yield amounts to 21.5–22 g. (95.5–98 per cent of the theoretical amount) of a product melting at 141–143°.

*D. Methionine.*—A suspension of 21.5 g. (0.063 mole) of this tricarboxylic acid in 350 cc. of hot water is heated on the steam bath and 40 cc. of concentrated hydrochloric acid (sp. gr. 1.19) is added. Carbon dioxide is immediately evolved and the substance goes into solution. After heating for one and a half hours, 200 cc. more of concentrated hydrochloric acid is added and heating is continued for forty-five minutes longer. The solution, on cooling, deposits phthalic acid; this is filtered off and washed with two 50-cc. portions of water (Note 3). The combined filtrate and washings are evaporated to dryness on the steam bath under reduced pressure, and the dry residue is dissolved in



50 cc. of hot water. The resulting solution is treated with 18 cc. of pyridine and poured into 150 cc. of hot absolute alcohol. Methionine rapidly crystallizes out; after cooling it is filtered, washed with alcohol, and dried. The first crop weighs about 6.9 g. The mother liquor is evaporated to dryness; the residue is taken up in 15 cc. of hot water and poured into 50 cc. of absolute alcohol, when a further 1.3 g. is obtained. The total 8.2 g. of nearly pure methionine is suspended in 200 cc. of boiling absolute ether, filtered, and dried. In this way, 7.9–8.0 g. of methionine (84–85 per cent of the theoretical amount), melting at 279–280° (corr.), is obtained.

## 2. Notes

1. The ethyl sodium phthalimidomalonate crystallizes with 1.5 molecules of alcohol, which is removed only on heating above 140° *in vacuo*.

2. About 10–12 g. of a pure product can be recovered by redistilling the distillate.

3. The phthalic acid thus recovered melts at 188° and weighs about 7.8 g. (75 per cent of the theoretical amount). Unless most of the phthalic acid is removed at this point, trouble may be encountered by the separation of pyridine phthalate with the methionine.

## 3. Methods of Preparation

*dl*-Methionine was first synthesized<sup>1</sup> by the Strecker method, but in very low yield. The above procedure, based on the directions published by the submitters,<sup>2</sup> has the advantage over the process of Windus and Marvel<sup>3</sup> in giving a much higher yield (54–60 per cent as against 13–19 per cent, based on the  $\beta$ -chloroethyl methyl sulfide consumed).

<sup>1</sup> Barger and Coyne, *Biochem. J.* **22**, 1417 (1928).

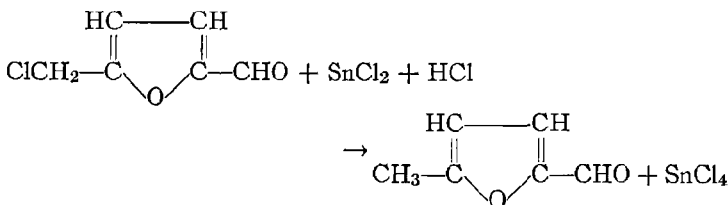
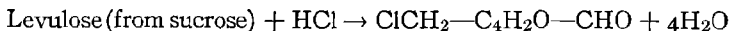
<sup>2</sup> Barger and Weichselbaum, *Biochem. J.* **25**, 997 (1931).

<sup>3</sup> Windus and Marvel, *J. Am. Chem. Soc.* **52**, 2575 (1930).



# XXI

## 5-METHYLFURFURAL



Submitted by I. J. RINKES.

Checked by JOHN R. JOHNSON and A. T. BLOMQUIST.

### 1. Procedure

IN a 12-l. round-bottomed flask fitted with a cork bearing a thermometer and a large bent glass tube, is placed 6 l. of 32 per cent hydrochloric acid (sp. gr. 1.163) (Note 1). The acid is heated to 50°, and 1 kg. (2.92 moles) of powdered sugar (Note 2) is dissolved in the liquid with shaking. The dark-colored solution is heated rapidly to 70–72°, kept at this temperature for ten minutes, and poured at once onto 3 kg. of cracked ice in a large earthenware crock (preferably in a hood). When the mixture has cooled to room temperature, 600 g. (2.67 moles) of commercial stannous chloride crystals ( $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ ) is added. The reaction mixture is stirred thoroughly for ten minutes and then allowed to stand for twenty-four hours.

The following day the acid liquid is filtered with suction through a large Büchner funnel, to remove large quantities of humus which are produced. The humus on the filter is washed with two 350-cc. portions of water and finally with two 300-cc. portions of benzene. The filtered liquid and aqueous washings have a volume of approximately 10 l. The 5-methylfurfural is

removed from the aqueous layer by extraction with benzene, using three 300-cc. portions of the solvent for each 2 l. of liquid (Note 3). The combined benzene extracts (about 5000 cc.) are divided into two or three portions and each is washed with two 150-cc. portions of 5 per cent sodium carbonate solution and two 100-cc. portions of water. The benzene solution is dried with 100-150 g. of anhydrous magnesium sulfate (or sodium sulfate) and the benzene is removed by distillation from a 1-l. flask provided with a short fractionating column and a separatory funnel for the continuous introduction of the solution. The distillation is stopped when the temperature of the distilling vapor reaches 85°.

The residue is transferred to a 250-cc. Claisen flask; two small portions of benzene (5-10 cc.) are used to rinse the last drops of the residue into the flask. The last traces of benzene are removed by warming gently under reduced pressure, and the 5-methylfurfural is then collected at 83-85°/15 mm. (Note 4). The yield is 63-70 g. (20-22 per cent of the theoretical amount, based upon the levulose portion of the sugar) (Note 5).

## 2. Notes

1. Commercial hydrochloric acid gives as satisfactory results as the chemically pure grade. The concentration of the hydrochloric acid should not exceed 32 per cent (sp. gr. 1.163) since stronger acid causes frothing during the heating and gives somewhat lower yields (56-57 g.).

Lengthening the time of heating or raising the temperature above 72° is definitely harmful.

2. Ordinary confectioners' sugar (XXXX sugar) was used. This contains 3 per cent of starch but the latter has no harmful effect.

3. The extractions should be carried out immediately after filtration since further quantities of humus are deposited if the liquid is allowed to stand.

4. 5-Methylfurfural discolors rapidly on standing, and after some time becomes quite black. The usual anti-oxidants do not retard this alteration perceptibly.

5. 5-Methylfurfural may be prepared by a modification of this method, which is more rapid but gives lower yields.<sup>1</sup> A solution of 800 g. of sucrose in 1 l. of hot water is allowed to flow slowly into a boiling solution of 500 g. of stannous chloride crystals, 2 kg. of sodium chloride, and 4 l. of 12 per cent sulfuric acid in a 12-l. flask. The aldehyde distils off as rapidly as it is formed and is steam-distilled from the original distillate after rendering it alkaline with sodium carbonate. The product is isolated by benzene extraction of the second distillate and distillation under reduced pressure. The yield is 27-35 g. (10-13 per cent of the theoretical amount).

### 3. Methods of Preparation

5-Methylfurfural has been prepared by the distillation of rhamnose with dilute mineral acids<sup>2</sup> and by the reduction of 5-bromo- and 5-chloromethylfurfural with stannous chloride.<sup>3</sup> The above procedure, starting from sucrose, has been published by Rinkes.<sup>4</sup>

<sup>1</sup> Scott and Johnson, J. Am. Chem. Soc. **54**, 2553 (1932).

<sup>2</sup> Maquenne, Ann. chim. phys. [6] **22**, 91 (1891); Runde, Scott, and Johnson, J. Am. Chem. Soc. **52**, 1288 (1930).

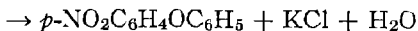
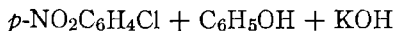
<sup>3</sup> Fenton and Gostling, J. Chem. Soc. **79**, 811 (1901).

<sup>4</sup> Rinkes, Rec. trav. chim. **49**, 1123 (1930); **52**, 337 (1933).



## XXII

### *p*-NITRODIPHENYL ETHER



Submitted by RAY Q. BREWSTER and THEODORE GROENING.

Checked by W. W. HARTMAN and J. B. DICKEY.

#### 1. Procedure

ONE HUNDRED SIXTY grams (1.70 moles) of a good grade of phenol and 80 g. (1.43 moles) of potassium hydroxide are placed in a 2-l. flask, and the mixture is heated to 130–140° until all of the alkali has dissolved. The potassium phenoxide is cooled to 100–110°, and 0.5 g. of copper catalyst (Note 1) and 78.8 g. (0.5 mole) of *p*-nitrochlorobenzene are added. The flask is then fitted with a mechanical stirrer, thermometer, and a reflux condenser. The stirrer is started, and the contents of the flask are warmed with a Bunsen burner to 150–160°, at which temperature a spontaneous reaction begins with ebullition and the separation of potassium chloride. The flame should be removed during this stage of the reaction. Boiling nearly ceases within five to seven minutes and another 78.8 g. (0.5 mole) of *p*-nitrochlorobenzene is added. The mixture is again heated as before until a second spontaneous reaction begins. This also proceeds for about five minutes without the application of heat. When boiling due to the exothermic reaction has ceased, heat is applied and a temperature of 150–160° is maintained for an additional thirty minutes. The dark-colored melt is then poured into 1.5 l. of ice water containing 50 g. of sodium hydroxide and stirred well for the removal of excess phenol. The crude *p*-nitrodiphenyl ether separates as a dark brown crystalline mass which is allowed to settle. The product is filtered on a Büchner funnel, washed with 2 l. of water, and pressed as free from water as possible. After drying in the air it is distilled from a 500-cc. Claisen flask. The small fraction boiling up to 170°/8 mm., which contains

*p*-nitrochlorobenzene, is discarded. A fraction boiling at 170–188°/8 mm. and weighing 14 g. is collected (Note 2). The main fraction boiling at 188–193°/8 mm. boils at 188–190°/8 mm. on redistillation with no forerun and practically no residue. *p*-Nitrodiphenyl ether solidifies on cooling to diamond-shaped crystals melting at 56–58°. The yield is 173–177 g. (80–82 per cent of the theoretical amount). Other nitrodiphenyl ethers may be prepared by this method (Note 3).

## 2. Notes

1. An active copper powder can be prepared from copper sulfate. One hundred grams (0.4 mole) of copper sulfate ( $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ ) is dissolved in 350 cc. of hot water in a 1-l. beaker. After cooling to room temperature 35 g. (0.53 gram atom) of zinc dust (more if necessary) is gradually added until the solution is decolorized. The precipitated copper is washed by decantation with water. Dilute hydrochloric acid (5 per cent) is added to the precipitate to remove the excess of the zinc, and agitation is continued until the escape of hydrogen ceases. The copper powder is filtered, washed with water, and kept in a moist condition in a carefully stoppered bottle.

2. The fraction boiling at 170–188°/8 mm. on redistillation yields 4 g. of *p*-nitrodiphenyl ether.

3. A yield of 84 per cent of *o*-nitrodiphenyl ether boiling at 183–185°/8 mm. is obtained when *o*-nitrochlorobenzene is used. For the preparation of *m*-nitrodiphenyl ether, the method of Ullmann and Sponagel,<sup>1</sup> using *m*-bromonitrobenzene, seems to be the best, since *m*-chloronitrobenzene gives large amounts of tarry matter.

## 3. Methods of Preparation

*p*-Nitrodiphenyl ether has been prepared by heating *p*-nitrochlorobenzene with potassium phenoxide and phenol<sup>2</sup> and by the nitration of diphenyl ether.<sup>3</sup>

<sup>1</sup> Ullmann and Sponagel, Ber. **38**, 2211 (1905).

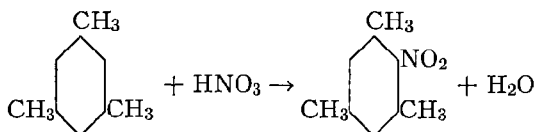
<sup>2</sup> Haeussermann and Teichmann, Ber. **29**, 1446 (1896).

<sup>3</sup> Suter, J. Am. Chem. Soc. **51**, 2583 (1929).



## XXIII

## NITROMESITYLENE



Submitted by GARFIELD POWELL and F. R. JOHNSON.

Checked by W. W. HARTMAN and J. B. DICKEY.

## 1. Procedure

IN a 500-cc. three-necked, round-bottomed flask provided with a mechanical stirrer, a dropping funnel, and a thermometer well, are placed 40 g. (0.333 mole) of mesitylene (Org. Syn. Coll. Vol. 1, 334) and 60 g. (55.5 cc.) of acetic anhydride (Note 1). The flask is placed in a bath of ice and water, and, when the reaction mixture is cold (below 10°), addition is begun of a mixture of 31.5 g. (20.8 cc., 0.5 mole) of fuming nitric acid (sp. gr. 1.51) in 20 g. (19.1 cc.) of glacial acetic acid and 20 g. (18.5 cc.) of acetic anhydride (Note 2). The nitric acid solution is added with stirring over a period of forty minutes, keeping the temperature between 15° and 20°.

When the addition of the nitric acid solution is complete, the reaction mixture is removed from the ice bath and allowed to stand at room temperature for two hours. The flask is then warmed, with shaking, to 50° on a water bath (Note 3) and maintained at that temperature for ten minutes. The cooled reactants are then poured slowly into 800 cc. of ice water and well stirred. About 40 g. of sodium chloride is added, and the aqueous layer is decanted and extracted with 200–250 cc. of a commercial grade of ether. The ethereal extract is added to the residual nitromesitylene, and this ethereal solution is washed

with three or four 30-cc. portions of a 10-15 per cent sodium hydroxide solution until the water extract is distinctly alkaline. The ether is then distilled, using a steam bath, and the residue is steam-distilled in the presence of 150 cc. of 10 per cent sodium hydroxide. The whole of the distillate (about three hours of steam distillation, collecting 1500 cc. of distillate) is collected (Note 4). The nitromesitylene settles to the bottom of the distillate. The water is decanted through a filter paper, and the residue is dissolved in 30 cc. of ether. The filter paper, if it contains any solid particles, is washed with 10 cc. of ether, and the two fractions are combined and placed in a 150-cc. distilling flask with water-cooled receiver. After removal of the ether on a steam bath, the yellow residue is distilled with a free flame. Almost the whole of the product distils at 243-250°. There is a residue of 0.5 to 1.5 g. The yellow crystalline product thus obtained weighs 47 g. It is purified by dissolving in 25 cc. of commercial methyl alcohol and cooling with stirring in a bath of ice and salt. The crystals are then filtered on a small Büchner funnel and washed twice with 5-cc. portions of cold methyl alcohol. From the wash alcohol, by exactly the same procedure, there is obtained 6-8 g. of crude crystals boiling at 243-249°/760 mm., which yields on crystallization 4 g. of pure nitromesitylene. The pure nitromesitylene, which has a light yellow color, melts at 43-44°. The yield is 41-42 g. (74.6-76.5 per cent of the theoretical amount).

## 2. Notes

1. A commercial grade of 85 per cent acetic anhydride is of sufficient purity.
2. The nitric acid is added with care to the acetic acid-acetic anhydride solution, keeping the temperature below 20° by means of a bath of ice and salt. An **explosive** reaction will take place if the nitric acid is added too rapidly.
3. A higher temperature is not advisable.
4. At the end of the steam distillation, a test sample should be clear and not contain oil droplets.

### 3. Methods of Preparation

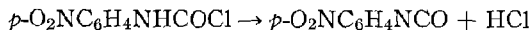
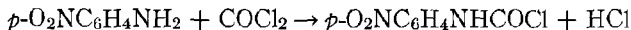
Nitromesitylene has been prepared by the direct nitration of mesitylene with concentrated nitric acid,<sup>1</sup> and by the action of benzoyl nitrate on mesitylene in carbon tetrachloride at low temperature.<sup>2</sup>

<sup>1</sup> Ladenburg, Ber. **7**, 1135 (1874); Fittig and Storer, Ann. **147**, 1 (1868); Biedermann and Ledoux, Ber. **8**, 58 (1875); Schultz, ibid. **17**, 477 (1884); Bamberger and Rising, ibid. **33**, 3625 (1900).

<sup>2</sup> Francis, Ber. **39**, 3801 (1906).



## XXIV

***p*-NITROPHENYL ISOCYANATE**

Submitted by R. L. SHRINER, W. H. HORNE, and R. F. B. COX.

Checked by W. W. HARTMAN and J. B. DICKEY.

**1. Procedure**

THE apparatus is shown in Fig. 2. Phosgene is introduced at one end of the apparatus, and gentle suction is applied at the other. In the 5-l. flask, A, 500 cc. of dry ethyl acetate (Note 1) is saturated with phosgene at room temperature. The phosgene is purified by bubbling it through cottonseed oil, B, to remove chlorine, and then through concentrated sulfuric acid, C, as shown in the figure (Note 2). A solution of 150 g. (1.09 moles)

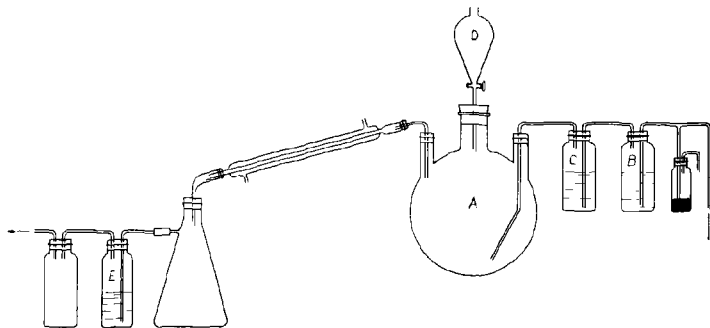


FIG. 2.

of *p*-nitroaniline in 1500 cc. of dry ethyl acetate is run in slowly from the separatory funnel, D, over a period of three to four hours. The addition of the *p*-nitroaniline solution must be at such a rate that the precipitate of *p*-nitroaniline hydrochloride that is

formed at first is allowed to dissolve and not accumulate (Note 3). During this time a steady stream of phosgene is passed through the solution to insure an excess (Note 4). Towards the end of the reaction, the solution must be boiled gently with a Bunsen flame to break up the lumps of *p*-nitroaniline hydrochloride which otherwise dissolve very slowly.

After the addition of the last of the *p*-nitroaniline, the stream of phosgene is continued for five minutes and then shut off. The flame under the flask is then turned up and the ethyl acetate distilled. Care must be taken at the end not to overheat the residue. The brown residue (Note 5) is treated with 800 cc. of hot dry carbon tetrachloride, and the insoluble residue (the di-substituted urea) is removed by filtration.

About two-thirds of the carbon tetrachloride is distilled. The solution is cooled, and the crystals of *p*-nitrophenyl isocyanate are filtered as quickly as possible in order to avoid prolonged exposure of the compound to the moisture of the air. By concentration of the mother liquor a further crop is obtained. The product is recrystallized from dry carbon tetrachloride and is obtained in the form of light yellow needles melting at 56–57° (Note 6). The yield after one recrystallization is 152–170 g. (85–95 per cent of the theoretical amount) (Note 7).

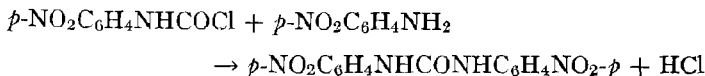
## 2. Notes

1. The ethyl acetate, free from ethyl alcohol, is dried with anhydrous magnesium sulfate.

2. This arrangement permits the phosgene reaction to be carried out conveniently and without danger, provided that a good hood and an exhaust fan are available. A slight vacuum is maintained in the system. The excess phosgene is absorbed in 20 per cent sodium hydroxide solution, E.

3. The mixture may be warmed if necessary to dissolve the *p*-nitroaniline hydrochloride.

4. The excess of phosgene retards the following reaction:



5. The crude residue is a mixture of *p*-nitroaniline hydrochloride, *p*-nitrophenyl carbamyl chloride, *p*-nitrophenyl isocyanate, and the *p,p'*-dinitrodiphenylurea. The *p*-nitrophenyl carbamyl chloride is converted to *p*-nitrophenyl isocyanate during recrystallization from the hot carbon tetrachloride.

6. The freshly prepared material melts at 56–57° but after storage soon starts to melt at 54°, particularly if the bottle in which it is stored is opened occasionally. In contact with the moisture of the air, *p,p'*-dinitrodiphenylurea is formed (m.p. 360°). This reaction with water is avoided if the material is sealed in a glass container.

7. *p*-Nitrophenyl isocyanate distils undecomposed at 160–162°/18 mm.

### 3. Methods of Preparation

*p*-Nitrophenyl isocyanate has been prepared by heating *p*-nitrophenyl carbamyl chloride. The latter has been obtained by the action of phosgene on *p*-nitroaniline in benzene-toluene solutions,<sup>1</sup> and by the action of phosphorus pentachloride on methyl *p*-nitrophenylcarbamate.<sup>2</sup> The preparation given above is based upon recent publications of the authors.<sup>3</sup>

<sup>1</sup> Vittenet, Bull. soc. chim. [3] **21**, 586 (1899); Van Hoogstraten, Rec. trav. chim. **51**, 414 (1932).

<sup>2</sup> Swartz, Am. Chem. J. **19**, 318 (1897).

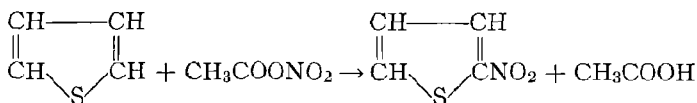
<sup>3</sup> Shriner and Cox, J. Am. Chem. Soc. **53**, 1601 (1931); Horne and Shriner, *ibid.*, **53**, 3186 (1931).





## XXV

## NITROTHIOPHENE



Submitted by V. S. BABASINIAN.

Checked by ROGER ADAMS and A. E. KNAUF.

## 1. Procedure

EIGHTY-FOUR grams (1 mole) of thiophene (Org. Syn. 12, 72) is dissolved in 340 cc. of acetic anhydride, and 80 g. (1.2 moles) of fuming nitric acid (sp. gr. 1.51) is dissolved in 600 cc. of glacial acetic acid (Note 1). Each solution is divided into two equal parts. One-half of the nitric acid solution is introduced into a 2-l. three-necked, round-bottomed flask, provided with a thermometer, a motor stirrer, and a separatory funnel. The mixture is cooled to 10°. Then with moderate stirring one-half of the thiophene solution is introduced, drop by drop, and at such a rate as to prevent the heating of the reaction mixture above the room temperature. A rapid rise of temperature will occur during the addition of the first fraction of the thiophene solution. In cool weather the temperature is controlled by dipping the nitrating flask into a bath of cold tap water. Cooling to a very low temperature is not necessary. Care should be taken to avoid superheating the reaction mixture (Note 2). After the addition of the first half of the thiophene, the temperature of the reaction mixture is reduced to 10° and the remainder of the nitric acid solution is rapidly introduced into the flask. Nitration is continued by the gradual addition of thiophene. Throughout the nitration the solution should show a permanent light brown color. The appearance of a pink or dark red color indicates

oxidation. The product is allowed to remain at room temperature for two hours. It is then treated with an equal weight of finely crushed ice with rapid shaking. Mononitrothiophene will begin to separate out in pale yellow crystals. More crystals will form if the mixture is allowed to remain in the ice chest for twenty-four hours or longer. It is filtered (Note 3) on a Büchner funnel or a Jena glass filter plate at a low temperature, washed thoroughly with ice water, pressed and dried in a brown desiccator or in the absence of light (Note 4).

The filtrate and the washings contain in solution a small quantity of the product. This is recovered by distillation with steam. The acid distillate will consist of snow-white crystals (if it is protected from light) and a solution of the compound. The solid is removed by filtration and washed. The filtrate is made neutral with sodium carbonate and extracted with ether. Upon drying and evaporating the ethereal layer will yield mononitrothiophene contaminated with dinitrothiophene (Note 5).

If the nitration is carried out in accordance with this outline, the product will be crystalline and pale yellow in color. The color is due to traces of dinitrothiophene and the other impurities. Mononitrothiophene has been crystallized by earlier workers from ether, alcohol, benzene, and other solvents. As a rule these solvents fail to yield a snow-white product. It has been found in this work that petroleum ether (b.p. 20–40°) possesses decided advantages in that by prolonged refluxing it extracts mononitrothiophene but does not readily dissolve the impurities. With petroleum ether, snow-white crystals have been obtained in needles 10 to 20 cm. in length.

The yield of the product melting at 44–45° is 90–110 g. (70–85 per cent of the theoretical amount). When purified by steam distillation and repeated crystallization it melts at 45.5° (Note 6).

## 2. Notes

1. The two acids should be mixed gradually, adding the first acid to the second with shaking. Cooling is often necessary.
2. Success will largely depend upon the proper control of

temperature. No trouble may be anticipated if the reaction mixture responds readily to the cooling effect of a cold water bath.

3. Mononitrothiophene is an active poison.<sup>1</sup> The accidental contact of an ethereal solution with the skin has produced painful blisters. In case of accident the compound should be removed from the exposed surface by washing with alcohol.

4. Earlier workers<sup>2</sup> have noted that the compound is sensitive toward light.

5. In order to detect the presence of dinitrothiophene, a few crystals of the solid are dissolved in alcohol and treated with a drop of weak solution of alcoholic potassium hydroxide. A pink or deep red color will develop at once. An excess of potassium hydroxide will destroy the color.<sup>3</sup>

6. Meyer and Stadler<sup>4</sup> state that nitrothiophene distills without decomposition at 224–225°.

### 3. Other Methods of Preparation

Nitrothiophene has been obtained along with dinitrothiophene by drawing a vigorous stream of air charged with thiophene through red fuming nitric acid.<sup>2</sup> It has also been prepared by nitrating thiophene between 0° and 5° with a mixture of acetic anhydride and fuming nitric acid.<sup>5</sup>

<sup>1</sup> Meyer, Ber. **18**, 1772 (1885).

<sup>2</sup> Meyer and Stadler, *ibid.* **17**, 2648 (1884).

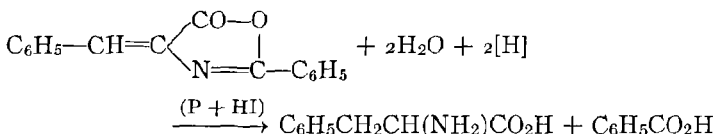
<sup>3</sup> Meyer and Stadler, *ibid.* **17**, 2780 (1884).

<sup>4</sup> Meyer and Stadler, *ibid.* **17**, 2649 (1884).

<sup>5</sup> Steinkopf and Lützendorf, Ann. **403**, 27 (1914); Ger. pat. 255,394 [Frdl. **12**, 144 (1912)].



## XXVI

***dl*-β-PHENYLALANINE**

Submitted by H. B. GILLESPIE and H. R. SNYDER.

Checked by W. W. HARTMAN and J. B. DICKEY.

**1. Procedure**

In a 1-l. three-necked, round-bottomed flask fitted with a reflux condenser, a mechanical stirrer, and a dropping funnel (Note 1) are placed 25 g. (0.1 mole) of the azlactone of α-benzoylamino-cinnamic acid (Notes 2, 3), 20 g. (0.64 gram atom) of red phosphorus, and 135 g. (125 cc.) of acetic anhydride. During a period of about one hour 195 g. (125 cc., 0.76 mole) of 50 per cent hydriodic acid (sp. gr. 1.56) is added with stirring (Note 4). The mixture is refluxed for three to four hours and, after cooling, is filtered with suction. The unreacted phosphorus is washed on the filter with two 5-cc. portions of glacial acetic acid, and discarded. The filtrate and washings are evaporated to dryness under reduced pressure, in a 500-cc. Claisen flask heated in a water bath. A 250-cc. distilling flask cooled in ice is used as a receiver, and the distillate is reserved for a second reduction (Note 5).

To the dry residue in the Claisen flask 100 cc. of water is added and the evaporation to dryness is repeated. The second distillate is discarded. To the residue in the flask 150 cc. of water and 150 cc. of ether are added and the mixture is shaken until solution is complete. The aqueous layer is separated and extracted three times with 100-cc. portions of ether. The ether

extracts are discarded; the water solution is heated on a steam bath with 2-3 g. of Norit and a trace of sodium sulfite until all dissolved ether has been removed. The solution is filtered, and the filtrate is heated to boiling and neutralized to congo red with 15 per cent ammonia (sp. gr. 0.94). Usually about 25 cc. of ammonia is required. The phenylalanine separates in colorless plates, which when cold are filtered and washed thoroughly on the filter with two 30-cc. portions of cold water. The yield is 10.5-11 g. (63.6-67 per cent of the theoretical amount) of a product which decomposes at 284-288° (corr.) (Note 6).

## 2. Notes

1. Clean corks protected by tin foil should be used.

2. This azlactone is prepared readily from benzaldehyde according to the procedure given for the azlactone of  $\alpha$ -benzoylamino- $\beta$ -(3,4-dimethoxyphenyl)-acrylic acid (Org. Syn. **13**, 8). From 53 g. (0.5 mole) of benzaldehyde, 89.5 g. (0.5 mole) of hippuric acid, 41 g. of fused sodium acetate, and 153 g. of acetic anhydride there is obtained 78-80 g. (62-64 per cent yield) of an almost pure product melting at 165-166° (corr.). This material is sufficiently pure for use in the preparation of phenylalanine. By crystallization from 150 cc. of benzene a product melting at 167-168° (corr.) is obtained.

3. The reduction may be carried out by the same procedure starting from  $\alpha$ -benzoylaminocinnamic acid, and in this way slightly higher yields are obtained. The azlactone may be converted into the free acid in the following way.

In a 12-l. flask fitted with a mechanical stirrer, 62.3 g. (0.25 mole) of the azlactone is suspended in 6 l. of water, and 11 g. (0.275 mole) of sodium hydroxide is added as a 10 per cent solution. The mixture is heated on the steam bath with stirring until solution is complete. This requires three to four hours. The hot solution is filtered and acidified with hydrochloric acid. The  $\alpha$ -benzoylaminocinnamic acid separates as white prisms in the hot solution, and when cold it is filtered. The yield is 55.5-64.5 g. (83-96.5 per cent) of almost pure product melting

with decomposition over a  $2^{\circ}$  range between the limits  $224^{\circ}$  and  $236^{\circ}$  (corr.). The crude acid can be recrystallized from alcohol, but its melting point remains unchanged.

4. During the addition the reaction mixture may solidify. If this occurs the stirrer is stopped and one or two portions of about 5 cc. of the hydriodic acid solution are stirred into the cake with a glass rod. The mass then becomes sufficiently fluid to permit use of the mechanical stirrer.

5. For a second run the distillate is placed in a 1-l. flask with 4 cc. of water, 25 g. of the azlactone, and 20 g. of red phosphorus. The mixture is refluxed for three to four hours and treated according to the above procedure. The yield is practically the same as in the first case.

6. The decomposition temperature is extremely variable and depends upon the rate of heating. The temperatures reported here were obtained by immersing the melting-point tube in a bath preheated to  $200^{\circ}$ , and then heating rapidly.

### 3. Methods of Preparation

*dl*-Phenylalanine has been prepared by the action of ammonia and hydrogen cyanide upon phenylacetaldehyde,<sup>1</sup> by the reduction of the oxime of phenylpyruvic acid,<sup>2,3</sup> by the action of ammonia on  $\alpha$ -bromo- $\beta$ -phenylpropionic acid,<sup>4</sup> and by the reduction of  $\alpha$ -aminocinnamic acid or its derivatives by means of sodium amalgam with water,<sup>5,6</sup> or red phosphorus with hydriodic acid.<sup>7,8</sup>

<sup>1</sup> Erlenmeyer and Lipp, Ann. **219**, 194 (1883).

<sup>2</sup> Erlenmeyer, *ibid.* **271**, 169 (1892).

<sup>3</sup> Knoop and Hoeseli, Ber. **39**, 1479 (1906).

<sup>4</sup> Fischer, *ibid.* **37**, 3064 (1904).

<sup>5</sup> Erlenmeyer, Ann. **275**, 1 (1893).

<sup>6</sup> Plöchl, Ber. **17**, 1623 (1884).

<sup>7</sup> Harington and McCortney, Biochem. J. **21**, 854 (1927).

<sup>8</sup> Lamb and Robson, Biochem. J. **25**, 1234 (1931).





## APPENDIX

### LATER REFERENCES TO PREPARATIONS IN THE PRECEDING VOLUMES

(The following references are to methods of possible preparative value that have recently been described. The numbers in parentheses following the name of the compound refer to the volume and page of *Organic Syntheses*.)

#### **Acetamide** (Coll. Vol. 1, 3):

From formamide by the action of hydrogen at 200–500°. Fr. pat. 708,084 [C. A. 26, 995 (1932)].

#### **Benzalacetophenone** (Coll. Vol. 1, 71):

From benzaldehyde and acetophenone, using cobalt, copper, iron or nickel as catalyst. Ger. pat. 554,785 [C. A. 26, 6080 (1932)].

#### **Benzenesulfonyl Chloride** (10, 6):

From sodium benzenesulfonate and benzotrichloride. Brit. pat. 384,722 [C. A. 27, 4251 (1933)].

From thiophenol on treatment with chlorine and water. Ger. pat. 550,685 [C. A. 26, 4828 (1932)].

#### **Bromoacetone** (Coll. Vol. 1, 283; 10, 12):

From acetone in water and concentrated hydrochloric acid by addition of bromine. HUGHES, WATSON, and YATES, J. Chem. Soc. 1931, 3322.

#### ***iso*-Butyl Bromide** (13, 20):

By passing hydrogen bromide through *iso*-butyl alcohol.

LONGINOV and LERMAN, *Khim. Farm. Prom.* **1933**, 14 [C. A. **27**, 3443 (1933)].

***o*-Chlorobenzoic Acid** (10, 20):

By the action of chlorine on saccharin. P. BERTOLO and A. BERTOLO, *Gazz. chim. ital.* **62**, 487 (1932).

***p*-Chloromercuribenzoic Acid** (Coll. Vol. **1**, 153):

Melting point 273°. NESMEYANOV and MAKAROVA, *J. Gen. Chem. (U. S. S. R.)* **1**, 1162 (1931) [C. A. **26**, 5295 (1932)].

***o*-Chlorotoluene** (Coll. Vol. **1**, 163):

From *o*-toluidine by diazotization, using magnesium chloride in place of copper salts. *Bull. soc. ind. Rouen* **60**, 103 (1932).

**Cyclohexene** (Coll. Vol. **1**, 177):

From cyclohexanol in 96 per cent yield, using phosphoric acid as a catalyst. DEHN and JACKSON, *J. Am. Chem. Soc.* **55**, 4285 (1933).

**Desoxybenzoin** (12, 16):

By the action of four moles of benzylmagnesium chloride on one mole of benzamide. (Yield 77 per cent.) JENKINS, *J. Am. Chem. Soc.* **55**, 704 (1933).

**Diacetonamine Hydrogen Oxalate** (Coll. Vol. **1**, 191):

Acetone and ammonia are condensed in the presence of various "promoters." A 45 per cent yield of diacetonamine isolated as the hydrogen oxalate is claimed when acetone saturated with ammonia at 0° is allowed to stand twenty-four hours with 8.5 per cent of ammonium nitrate. SUZUKI and HORIE, *Bull. Inst. Phys.-Chem. Research (Tokyo)* **11**, 383 (1932). Abstract 30 (in English) published with *Sci. Papers Inst. Phys.-Chem. Research (Tokyo)* **18**, Nos. 350-4 [C. A. **26**, 4302 (1932)].

***p*-Dimethylaminobenzophenone** (Coll. Vol. 1, 211):

From benzanilide imidochloride, dimethylaniline, and aluminum chloride in carbon disulfide. SHAH and CHAUBAL, J. Chem. Soc. 1932, 650.

**Di-*p*-tolylmercury** (Coll. Vol. 1, 226):

From lithium tolyl and mercuric chloride. AUSTIN, J. Am. Chem. Soc. 54, 3726 (1932).

**Furan** (Coll. Vol. 1, 269):

From furoic acid. GILMAN and LOUSINIAN, Rec. trav. chim. 52, 156 (1933).

**Furoic Acid** (Coll. Vol. 1, 270):

By the oxidation of furfural with potassium dichromate and sulfuric acid in 75 per cent yield. HURD, GARRETT, and OSBORNE, J. Am. Chem. Soc. 55, 1084 (1933).

**Glutaric Acid** (10, 58):

From cyclopentanone with nitric acid. E. BOEDTKER, J. pharm. chim. 15, 225 (1932).

***dl*-Glyceric Aldehyde** (11, 50):

From acrolein by oxidation with sodium chlorate and osmium tetroxide. NEUBERG, Biochem. Z. 255, 1 (1932).

**Glycine** (Coll. Vol. 1, 293):

From sixty parts of ammonia to one part of chloroacetic acid in 59 per cent yield. KULIKOV and SLASTENINA, J. Gen. Chem. (U. S. S. R.) 2, 777 (1932) [C. A. 27, 2674 (1933)]. These authors could not check the procedure of ORTEN and HILL, J. Am. Chem. Soc. 53, 2797 (1931);

***n*-Heptyl Alcohol** (Coll. Vol. 1, 298):

From pentane and ethylene oxide in the presence of anhydrous aluminum bromide. Fr. pat. 716,604 [C. A. 26, 2198 (1932)].

***o*-Iodophenol** (Coll. Vol. 1, 319):

By the action of iodine in aqueous potassium iodide on *o*-chloromercuriphenol. CHI, Trans. Sci. Soc. China 7, 169 (1932) [C. A. 26, 5552 (1932)].

**Lauryl Alcohol** (10, 62):

From ethyl laurate by reduction with hydrogen under pressure with copper catalyst. Ger. pat. 552,888 [C. A. 26, 5573 (1932)].

***l*-Menthone** (Coll. Vol. 1, 333):

By heating 3-menthene oxide at 250° in contact with silica gel. Fr. pat. 723,395 [C. A. 26, 4063 (1932)].

**Mesitylene** (Coll. Vol. 1, 334):

By the methylation of commercial xylene and separation of the mesitylene from the mixture of hydrocarbons by crystallization of the sulfonate. SMITH and CASS, J. Am. Chem. Soc. 54, 1603 (1932).

**Methyl Amyl Ketone** (Coll. Vol. 1, 343):

From ethyl *n*-butylacetoacetate in 95 per cent yield, using phosphoric acid as a catalyst. DEHN and JACKSON, J. Am. Chem. Soc. 55, 4285 (1933).

**Pentaerythritol** (Coll. Vol. 1, 417):

Calcium hydroxide is a better catalyst at 40–90° than barium hydroxide, magnesium hydroxide, sodium hydroxide, and sodium carbonate for preparing pentaerythritol. CORBELLINI and

LANGINI, *Giorn. chim. ind. applicata* **15**, 53 (1933) [*C. A.* **37**, 4526 (1933)].

**Perbenzoic Acid** (Coll. Vol. **1**, 422):

From benzoyl chloride and sodium peroxide. B. T. BROOKS and W. B. BROOKS, *J. Am. Chem. Soc.* **55**, 4310 (1933).

**Phenylacetic Acid** (Coll. Vol. **1**, 427):

By the carbonation of benzyl magnesium chloride in 40 per cent yield. AUSTIN and JOHNSON, *J. Am. Chem. Soc.* **54**, 647 (1932).

**Phloroglucinol** (Coll. Vol. **1**, 444):

By the hydrolysis of 1,3,5-trichlorobenzene with superheated steam in the presence of silica gel. LLOYD and KENNEDY, *U. S. pat.* 1,899,844 [*C. A.* **26**, 2747 (1932)].

**Pinacolone** (Coll. Vol. **1**, 451):

From pinacol hydrate, using phosphoric acid as a catalyst. DEHN and JACKSON, *J. Am. Chem. Soc.* **55**, 4286 (1933).

**Quinizarin** (Coll. Vol. **1**, 464):

By treating anthraquinone with nitrosylsulfuric acid in the presence of mercury or a mercury compound. *Brit. pat.* 346,355 [*C. A.* **26**, 1948 (1932)].

By heating a mixture containing phthalic anhydride, boric acid, *p*-chlorophenol, and strong sulfuric acid to about 150° and then further raising the temperature and diluting with steam. *U. S. pat.* 1,845,632 [*C. A.* **26**, 2203 (1932)].

**Sodium *p*-Hydroxyphenylarsonate** (Coll. Vol. **1**, 477):

By the action of sodium arsenite on diazotized *p*-aminophenol. *Russ. pat.* 23,362 [*C. A.* **26**, 1946 (1932)].

**Styrene** (Coll. Vol. 1, 43):

By passing  $\alpha$ -chloroethylbenzene over active carbon at atmospheric pressure and at 260°. Ger. pat. 559,737 [C. A. 27, 737 (1933)].

**1,3,5-Trinitrobenzene** (Coll. Vol. 1, 526):

By the action of alcoholic ammonia on trinitrobenzaldehyde (quantitative yield). SECAREANU, Bull. soc. chim. [4] 51, 591 (1932).

## ADDITIONS AND CORRECTIONS FOR PRECEDING VOLUMES

(The numbers in parentheses following the name of the compound refer to the volume and page of Organic Syntheses.)

### ***n*-Butyryl Chloride** (Coll. Vol. 1, 142):

If the directions are followed exactly as given, large amounts of the anhydride are obtained. If, however, the thionyl chloride is kept cool in a water bath during the addition of the acid, practically no anhydride is obtained and the yield approaches 90 per cent.

R. R. READ, private communication.

### **Glutaric Acid** (Coll. Vol. 1, 283; 10, 58):

Glutaric acid is easily and cheaply prepared by oxidation of cyclopentanone; cf. Adipic Acid, Coll. Vol. 1, 18. The oxidation needs careful control—if it gets out of hand succinic acid results.

In a 2-l. round-bottomed, 3-necked flask fitted with a stirrer and two large-bore condensers are placed 200 cc. of 50 per cent nitric acid and 0.25 g. of vanadium pentoxide. The flask is heated to 65-70° in a water bath (thermometer in water), and 1 cc. of cyclopentanone added. Oxidation is indicated by the production of brown fumes. The water bath is removed, and 42 g. (less the 1 cc.) of the cyclic ketone added from a dropping funnel through the condenser at the rate of a drop every three seconds. The heat of the reaction keeps the flask at about 70°. If the temperature drops, oxidation ceases until the ketone has accumulated, when it may proceed almost explosively. In such a case, or if the temperature is higher, much succinic acid is formed. After addition has been completed, the water bath

is replaced and the mixture heated to boiling. The contents of the flask are poured into an evaporating dish (hood), and the volume reduced one-half. When cold, the acid is filtered and the operation repeated twice; the last time the acid is yellowish, and the color is removed by washing with dilute hydrochloric acid. The crude glutaric acid is white and weighs 50-55 g. (80-85 per cent); m.p. 92-94°. If any succinic acid is present owing to lack of proper control, it separates in the first crop. It is more convenient to allow the mother liquors from several runs to accumulate and work them up separately; from each run 2-3 g. more of glutaric acid may be so obtained.

Further purification is accomplished, if desired, by the original directions. The acid, as prepared above, always contains traces of nitric acid, but is satisfactory for conversion into the anhydride. If the catalyst is omitted, the yield is less by 10 per cent.

C. F. H. ALLEN and W. L. BALL, private communication.

### Heptyl Alcohol (Coll. Vol. 1, 298):

It has been frequently noted that certain lots of iron filings are not satisfactory for the reduction of heptaldehyde to heptyl alcohol in acetic acid solution. E. E. REID and J. R. RUHOFF have found that the addition of a solution of 20 g. of nickel chloride hexahydrate in 50 cc. of water immediately after the addition of the aldehyde will cause the reaction to start at once and will greatly accelerate the rate of reaction so that it is complete in two hours instead of the usual six to seven hours. The checkers have found this to be the case even with a lot of iron which could not be made to react when reduced in hydrogen. It is also recommended that the reaction mixture be divided between two 12-l. flasks and that 3 l. of water be added to each half immediately at the end of the reaction. This prevents the mixture from setting to a hard mass in case the steam distillation is not carried out at once, and also reduces the amount of foaming.

C. R. NOLLER and R. BANNEROT, private communication.



**Monochloromethyl Ether** (Coll. Vol. 1, 369):

Technical formalin contains 8-10 per cent of methyl alcohol, so that it is not possible to use the table of densities (Note 1 of the preparation) for determining the formaldehyde content of the solutions. For example, a solution containing 37 per cent of formaldehyde and 10 per cent of methyl alcohol would have a density of 1.09 and correspond to 28 per cent of formaldehyde in pure water. In view of this, the recorded yield should probably be 64-66 per cent instead of 86-89 per cent.

N. D. SCOTT, private communication.

## SUBJECT INDEX

(This Index Comprises Material from Volumes X to XIV of this Series)

(Names in small capital letters refer to the titles of preparations which are given in full detail. A number in ordinary bold face type denotes the volume. A number in bold face italics refers to a page which gives preparative directions for a substance formed either as principal product or as a by-product, or to a product which has been prepared by a method analogous to the one given. Other numbers in ordinary type indicate pages on which a compound is mentioned incidentally or information is given concerning an item other than a compound.)

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